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SURGICAL MANAGEMENT OF CARCINOMA OF THE MIDTHORACIC ESOPHAGUS*

Preliminary Report

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BOSTON

IN OCTOBER, 1942, in an address given before the American Academy of Ophthalmology and Otolaryngology, I[1] made the following statement:

> Adequate removal of a carcinoma located in the middle half of the esophagus precludes the possibility of performing an anastomosis within the chest for the restoration of continuity. In all these cases it is necessary to establish a cervical esophagostomy and a gastrostomy or enterostomy for feeding.

Two years later, as a result of increased experience with the transthoracic resection of carcinoma of the cardia and lower end of the esophagus, the field of resection followed by an anastomosis has been enlarged and a satisfactory technic for the removal of malignant lesions higher in the esophagus has been developed. The Torek procedure can therefore be discarded except in those relatively rare cases in which the lesion extends well above the aortic arch.

The Torek operation, originally described in 1913,[2] has had a limited use. There are two serious objections to this procedure. In the first place, if it is carried out according to Torek's original technic, which involves cutting across the lower esophagus and not entering the abdominal cavity, two important groups of lymph nodes to which these tumors frequently metastasize are not removed; these are the subdiaphragmatic periesophageal nodes and the group found in relation to the left gastric vessels (Fig. 1). As a result, the operation is hardly worth while because these nodes are so frequently involved (Table 1). If one takes into account the additional fact that the resectability of carcinoma in the midesophagus is perhaps the lowest of any region in the body, being found in only 14 per cent of all patients seen,[1] the possibility of obtaining a cure or a reasonably long remission of symptoms is discouragingly remote. The principal hope in such cases is for worth-while palliation.

TABLE 1. *Abdominal-Node Metastases in Carcinoma of the Esophagus (72 Autopsied Cases).*

LOCATION OF TUMOR	NO. OF CASES	ABDOMINAL NODES	
		POSITIVE	NEGATIVE
Upper third (neck and upper chest) ...	24	1	23
Middle third	32	11	21
Lower third	16	8	8

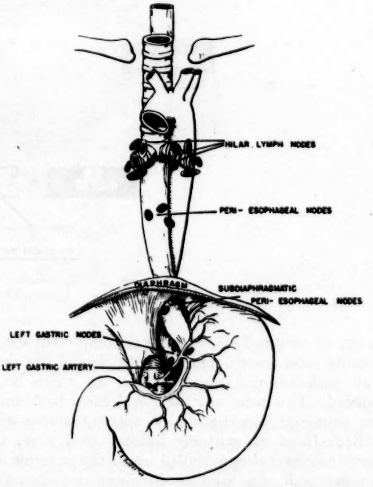

FIGURE 1. *The Most Frequent Sites of Lymph-Node Invasion in Cases of Carcinoma of the Esophagus (reproduced from Sweet,[3] by permission of the publisher).*

The second major objection to the Torek operation is that as a palliative procedure it is most unsatisfactory. The continuous discharge of saliva and mucus through the cervical esophagostomy stoma and the trouble attending the care and the use of the gastrostomy for feeding make the patients who have been subjected to this operation miserable

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and unhappy. If the use of a rubber-tube connection is attempted, there may be leakage around the tube, difficulty in keeping it adjusted and inability of the patient to eat anything but liquids because of the mechanical inadequacy of the system. Even if, after much effort on the part of the surgeon and with hope and fortitude on the part of the patient, an external plastic esophagus is constructed, the length of time required makes the procedure impractical. In some cases, by the time the patient is able to take a soft diet and swallow the food through such a tube, he is already suffering the effects of recurrent or metastatic disease.

Torek Procedure

Since January, 1940, Torek operations have been performed on 14 patients at the Massachusetts General and Palmer Memorial hospitals. There were 2 postoperative deaths and 12 survivals. In 4 cases, an external esophagus was completed, a connecting tube constructed from the skin of the chest wall with additional grafts from the thigh being utilized. This tube was used in 2 cases to connect the proximal esophagostomy opening above with a Beck-Jianu gastrostomy below. In 1 case, the lower esophageal end, pulled up to the anterior abdominal wall, was used as the lower stoma, and in 1 the fundus of the stomach and the stump of the esophagus were used after being pulled up under the skin of the chest wall.[1] Two patients died of metastases soon after the completion of the external esophagus. Two were alive and well 4 and 2 years, respectively, after operation. Of the remaining 8 patients, 4 died during the period of construction of the external esophagus — 1 of pneumonia that did not respond to sulfonamide chemotherapy, and 3 of metastases or local recurrences. The remaining 4 patients have died of their disease without any attempt's being made to construct an external esophagus (Fig. 2). These results have been discouraging.

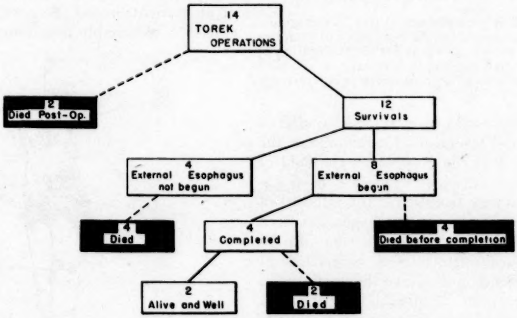

Figure 2. *Experience with the Torek Operation at the Massachusetts General Hospital.*

Resection Followed by High Esophagogastric Anastomosis

New hope has arisen from the application of knowledge gained from a large experience with resection of the cardia and lower esophagus by the transthoracic route. As a result, it is now possible to perform a much more radical esophagectomy in such cases, including the removal of the lymph nodes below the diaphragm, and to restore immediately the continuity of the gastrointestinal tract by an esophagogastric anastomosis performed high in the chest.

Technic of Operation

With the patient lying on his right side, the eighth rib on the left is resected and the seventh, sixth and, if necessary, fifth ribs are divided posteriorly. This incision provides an adequate exposure to the region of the growth, and at the same time gives room enough below for incision of the diaphragm and mobilization of the stomach so that it can be brought up for an anastomosis high in the thorax.

Because of their location so close to several vital structures, such as the aorta, the inferior pulmonary vein, the left main bronchus and the left pulmonary artery, many of the tumors in this location are inoperable owing to direct invasion of these structures. It is therefore best to explore first the region of the growth. If one is careful, the possibility of completely mobilizing the tumor-bearing portion of the esophagus can usually be determined before division of any of the segmental esophageal arteries, which arise from the aorta. Once the resectability of the growth has been established, these vessels can be cut and the entire mass freed. In carrying out the mobilization of the growth, an opening into the

right pleural cavity is often made. At times it is necessary to remove a portion of the mediastinal pleura of the right side because of its adherence to the growth. The anesthetist's positive pressure prevents any serious degree of collapse of the right lung in such cases, and no attempt to close the opening need be made, because once the chest-wall incision is made airtight by its closure, there is no further danger of collapse of either lung unless lung tissue has been injured so as to permit escape of air from the alveoli.

After the midesophagus has been completely mobilized, the diaphragm is incised from the costal insertion through the hiatus. The upper portion of the stomach is then mobilized by dividing the postthroughout its wall, especially at its upper portion. Furthermore, and for the same reason, the incision across the stomach must be at or just distal to the cardia, thus minimizing the danger of interrupting any anastomotic vascular channels within the stomach wall. Nevertheless, even in these cases one can with care remove the major portion of the lymph nodes around the cardia and from the region of the left gastric vessels.

Once the mobilization is complete, the stomach is cut across at or just below the cardia, its cut end is inverted, and a rubber glove is tied over the proximal end to avoid soiling the field of operation. If there is 5 cm. or more of normal esophagus between the aortic arch and the superior margin of the

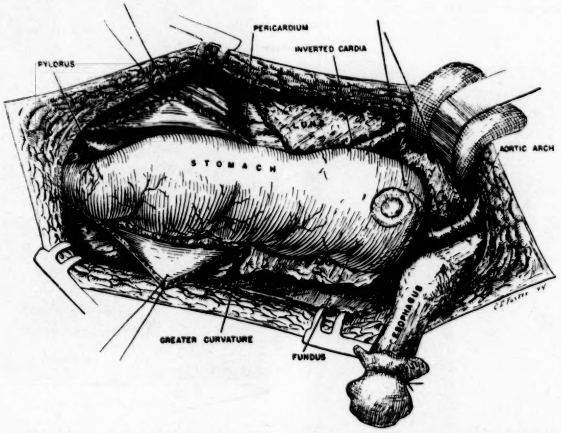

FIGURE 3. *High Esophagogastric Anastomosis for Carcinoma of the Midthoracic Esophagus (reproduced from Sweet,[5] by permission of the publisher).*

The esophagus has been completely mobilized and pulled out from behind the aortic arch. The stomach, after complete mobilization preserving the right gastric and right gastroepiploic vessels, is shown pulled high into the chest so as to make possible an anastomosis at or just above the level of the aortic arch.

cardial attachments, the vasa brevia, the gastrolienal and gastrohepatic ligaments and the left portion of the gastrocolic ligament. In all cases the ascending branches of the left gastric vessels must be severed to make it possible to swing the fundus far enough into the thorax to permit a high anastomosis.

In some cases in which the growth is unusually high, so that the esophagus must be divided close to or even above the aortic arch, it is necessary to divide the left gastric artery close at its origin and to cut the left gastroepiploic artery. I have proved by actual performance that this can be done with a successful outcome. The stomach must, however, be handled with great care to avoid trauma to any of the vessels that enter into the anastomosis

growth, it is usually possible to perform an esophagogastric anastomosis just below the aortic arch. If, on the other hand, the growth extends nearer to the arch, an anastomosis becomes impossible unless the esophagus is pulled up from behind and the anastomosis is performed in front of the aortic arch or at the level of its superior margin. In January of this year Garlock[3] reported such a case. The usual three-layer, silk-technic anastomosis is performed, with excision of a circular piece of the wall of the fundus of the stomach. The technical details of this operation have been described elsewhere.[4, 5]

This operation in cases of carcinoma of the midthoracic esophagus approaches more closely than anything previously available the ideal procedure for the radical removal of the tumor, including the

majority of the regional lymph nodes, for more satisfactory palliation in incurable cases, and for the obtaining of a better functional result.

Experience in Carcinoma of the Midthoracic Esophagus

Since we have learned how to free the stomach sufficiently to bring the fundus to the level of the aortic arch or even above it, resections followed by high anastomosis have been carried out in 9 patients at the Massachusetts General and Palmer Memorial hospitals. In 5 of these cases, the upper limit of the growth was at a level that made it possible to perform an esophagogastric anastomosis just below the aortic arch. One of these patients died suddenly of what was apparently coronary thrombosis (permission for autopsy was refused). One is still in the hospital. The remaining 3 were doing well a few months to somewhat over a year from the date of operation.

In the remaining 4 cases, it was impossible to perform an anastomosis below the aortic arch, so that the upper end of the esophagus had to be mobilized and pulled up in front of the arch (Figs. 3 and 4). The level of the completed anastomosis was at the superior margin of the aortic arch. Two of these patients died in the hospital, one because of sepsis resulting from tearing into an extremely adherent and actually inoperable growth during the operation, and the other because of coronary thrombosis (proved by autopsy). Of the 2 patients who survived the operation, one died subsequently of metastatic carcinoma, and the other recovered completely and resumed work.

As an illustration of what can be accomplished in cases of carcinoma of the midthoracic esophagus by this new operation, the last case mentioned is reported in detail.

C. K. (M. G. H. 444,523), a 63-year-old woman, was seen for the first time on May 17, 1944. For 4 months she had been having difficulty in swallowing, the trouble beginning with solids but gradually increasing until she could swallow nothing but liquids; even then she had to drink very slowly. She had lost a great deal of weight and strength.

Physical examination was essentially negative except for emaciation. The weight was 94 pounds. The heart sounds were regular and of good quality, with no murmurs. The blood pressure was 120/80. The diaphragm was low and moved only 1 cm. or less. Chest expansion was poor.

The patient was admitted to the Baker Memorial on May 19. On admission the white-cell count was 5400, the red-cell count 3,690,000, and the hemoglobin (photoelectric method) 11.0 gm. The nonprotein nitrogen was 32.5 mg. per 100 cc., the serum protein 6.0 gm., and the blood chloride 93 milliequiv. per liter. A blood Hinton test gave a negative reaction. X-ray examination revealed an ulcerating lesion in the middle

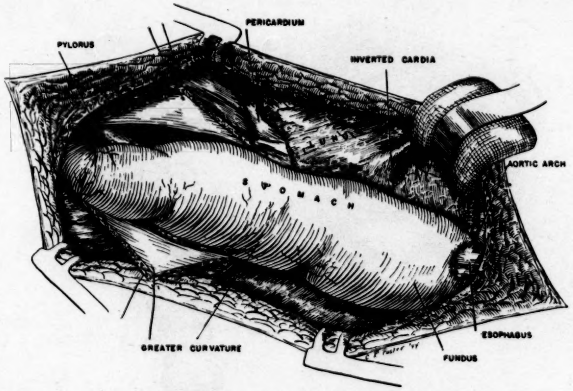

FIGURE 4. *The Completion of a High Anteaortic Esophagogastric Anastomosis (reproduced from Sweet,[3] by permission of the publisher).*

third of the esophagus, the appearance being consistent with a malignant tumor (Fig. 5).

Esophagoscopy, performed by Dr. Edward B. Benedict, showed an annular, proliferating, nodular mass arising mostly from the left wall of the midesophagus, apparently not fixed and only partially obstructing the lumen. Its appearance was characteristic of carcinoma. Biopsy specimens were reported by the pathologist as epidermoid carcinoma, Grade III.

Intravenous infusions of glucose in saline solution and of amino acids (Amigen), as well as transfusions of blood, were given. The patient was able to take a high-calorie liquid diet. Parenteral vitamins were administered by the intravenous route. During the 48 hours immediately preceding operation sulfadiazine was given.

At operation, performed on May 27, an oblique incision was made across the left side of the chest and the 8th rib was resected. To obtain adequate exposure the 7th, 6th and 5th ribs were divided posteriorly. The growth was found lying in the esophagus and extending from just below the level of the aortic arch to a point opposite the inferior pulmonary vein. It was densely adherent to the areolar tissues over the aorta, and at one point it was necessary to cut so close to the aorta that one of the esophageal arteries was cut flush with its wall. The bleeding from this vessel had to be controlled by means of two sutures of arterial silk. After much painstaking dis-

section the growth was freed from the aorta. It was dissected from the hilus of the lung with greater ease, although there was a certain amount of adhesion to the structures just behind the left main bronchus. After the midportion of the esophagus had been freed all the way above the aortic arch, it was decided that a resection could be carried out.

After the phrenic nerve had been pinched, the diaphragm was incised. The spleen was freed from the stomach by cut-

FIGURE 5. *Roentgenogram (Patient C. K.).*
The thoracic esophagus shows a filling defect caused by a carcinoma in the middle of the thoracic esophagus.

ting the vasa brevia and the left gastroepiploic vessels, the former of which were extremely short. There were two or three enlarged, hard lymph nodes in the region of the left gastric vessels, making it necessary to divide these vessels close to their origin to remove the nodes. Thus the stomach was entirely severed from its blood supply except for the right gastric and the right gastroepiploic vessels. A clamp was put across just distal to the cardia in such a way as to include all the involved lymph nodes in the excised portion. A second clamp was put on and the stomach was cut between them. A square of rubber dam was tied over the proximal cut edge. The distal edge was sutured, a fenestrated clamp being used. A second layer of catgut was used to invert the sutured edge, and a final layer of interrupted silk sutures was applied.

The stomach having been freed, it was possible to pull it up to a point just above the aortic arch. The esophagus was pulled up from behind the aortic arch and around in front of it. A circular incision was made close to the apex of the fundus of the stomach, and a three-layer, interrupted-silk, end-to-side anastomosis was carried out that after completion lay opposite the superior margin of the aortic arch. The stomach was fixed in the chest by interrupted silk sutures between it and the pleura lateral to the aorta. No attempt was made to close the opening that had been made in the right pleural cavity. The liver was palpated, nothing abnormal being found. The diaphragm was loosely attached to the stomach and the remaining portion of the diaphragm was closed. A catheter was led out through the lower part of the chest, its tip being placed behind the stomach in the right pleural cavity. A hole was made in the side of the catheter so as to drain the left pleural cavity, and after the lung had been expanded the chest was closed, using silver wire in the 7th rib to help maintain rigidity. The remainder of the wound was closed with silk.

Pathological examination showed the specimen to consist of a previously opened segment of esophagus 11 cm. long, with a 2 cm.-cuff of normal-appearing gastric mucosa. Five centimeters above the cardioesophageal junction was a firm ulcer 3 cm. in diameter that completely surrounded the esophageal wall; its base was reddish-gray and granular. The mucosa-covered ulcer margins were raised and indurated. The cut surface was grayish white and granular, and the lesion extended into the surrounding fascia. The upper border of the ulcer was 2 cm. from the esophageal incision line. In the portion of esophagus just distal to the main lesion, there were several small, indurated, yellowish brown, submucosal nodules measuring 3 to 5 mm. There were many shaggy, yellowish gray lymph nodes measuring 1 to 2 cm. scattered over the posterior aspect of the tissue, some of them hard and others cystic and necrotic on section. Eight of these were removed from various areas for section. Microscopical examination showed the tumor to be epidermoid carcinoma,

FIGURE 6. *Resected Specimen (Patient C. K.) (reproduced from Sweet,[5] by permission of the publisher).*
This includes the esophagus, which contains the tumor, the cardia and a portion of the fundus of the stomach. Three groups of enlarged lymph nodes can be seen attached to the gastric end of the specimen.

Grade III, with metastases to the regional lymph nodes (Fig. 6).

The patient's immediate recovery from operation was uneventful. During the first 4 days she experienced enough respiratory embarrassment to require the continuous use of an oxygen tent, but after that time there was no difficulty and the convalescence was free from complications.

The patient returned to work, and at the last examination, several months after operation, was well and had gained 12 pounds in weight.

Figures 7 and 8 are reproductions of postoperative roentgenologic films showing barium in the esophagus and stomach,

FIGURE 7. *Roentgenogram (Patient C. K.).*

This anteroposterior view, taken four months postoperatively, shows that the level of the esophagogastric anastomosis is considerably above that of the aortic arch and illustrates the fact that the major portion of the stomach lies within the chest.

The high level of the anastomosis opposite the manubrium of the sternum is shown especially in the lateral view (Fig. 8). Almost the entire stomach lies in the chest.

SUMMARY

The classic Torek operation is subject to the objections that it does not make provision for radical removal of the regional lymph nodes, which are so frequently invaded by disease, thus diminishing the possibility of obtaining a cure, and that it fails to provide satisfactory palliation because of the discomfort and unhappiness of the patient that result from the presence of a cervical esophagostomy and the necessity of being fed by gastrostomy. The construction of an external esophagus to connect the two stomas is a long and tedious process, usually performed in several stages, and can rarely be completed except in the most favorable cases.

Experience with 14 cases in which the Torek operation was performed is set forth.

Resection of the entire esophagus below the level of the aortic arch, followed by a high esophagogastric anastomosis either just below or just above the level of the aortic arch, offers a more nearly ideal solution of the problem of the surgical removal of carcinoma of the esophagus, since it facilitates radical removal of the tumor, including the majority of the regional lymph nodes, and provides a more satisfactory degree of palliation in incurable cases and a better functional result.

A summary of the results of this operation in 9 cases is given, and a case is reported in detail as an illustration of what can be accomplished with this relatively new procedure.

During the interval of time that has elapsed since this paper was read before the New England Surgical Society, 11 additional patients have been subjected to radical operation for carcinoma of the middle half of the thoracic portion of the

FIGURE 8. *Roentgenogram (Patient C. K.).*

The lateral view, also taken four months postoperatively, shows that the esophagogastric anastomosis is opposite the manubrium of the sternum.

esophagus. In 3 of these the anastomosis was performed just below the aortic arch, and in 8 of them the growth extended so high that it was necessary to perform the anastomosis above

the aortic arch. Recovery was uneventful in 8 cases; complications occurred in 3, and these patients died. The causes of death in these cases were chylous hydrothorax, empyema and cardiac failure, respectively. All deaths occurred in patients with high growths, which required anastomosis above the aortic arch.

The inclusion of these 11 additional cases makes a total series of 20 cases of carcinoma of the midthoracic esophagus with resection followed by high esophagogastric anastomosis. In 8 of these an anastomosis just below the aortic arch was performed, whereas in 12 it was necessary to relocate the esophagus and perform the anastomosis above the aortic arch.

In the entire series there were 6 deaths, a mortality of 30 per cent. Thirteen patients recovered and left the hospital in good condition, and 1 is still in the hospital.

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Discussion

Dr. Fred B. Lund, Boston: This is one of the most brilliant presentations I have ever heard. Some years ago I had an opportunity to see at the Nose and Throat Department of the City Hospital all the cases of cancer of the esophagus that came there, and of the 35 cases, 3 appeared to be operable. I operated on one patient through the chest; when I found that the growth had invaded the aorta, I did nothing more and the patient died. In the second case, I did a Torek operation, incising the pleura and sewing it up; the patient died. In the last case, I did a Lilienthal operation through the back and this patient also died. All these cases had presented poor prospects, but even so I was rather discouraged. Nevertheless I should have continued to operate if more operable cases had presented themselves.

Dr. Harlan F. Newton, Boston: It is well known to every one of us that the esophagus has been the "soft spot of the underbelly" of surgery. We have all heard and read of the splendid results in the surgical treatment of carcinoma of the upper third of the esophagus by excision that have in the past few years come from Canadian surgeons. Also, the lower third of the esophagus, attacked by cancer, has frequently been treated by excision with success. Dr. Sweet's paper deals with the surgical excision of carcinoma of the midesophagus, a tumor that has been considered up to this time as hopelessly inoperable. This makes his contribution outstanding and a pioneer piece of work.

The esophagus does not lend itself well to healing following operative trauma because of poor tissue resistance, friability, leaks following anastomoses, mediastinitis and other complications. Also of tremendous importance are the high degree of malignancy and the high incidence of early metastasis of practically every esophageal carcinoma.

Dr. Sweet is truly to be complimented both on this extraordinary series of cases so beautifully handled and for his modesty, for I know of no other such series of cases comprising surgical excision of carcinoma of the midesophagus. We operated on a patient at the Peter Bent Brigham Hospital who has now gone about fourteen months without recurrence after complete resection of the carcinoma; this tumor originally appeared to be inoperable, but it was really at the junction of the lower and middle thirds of the thoracic esophagus.

Technically, excision of the midthoracic esophagus with mobilization of the stomach and anastomosis of the upper end of the esophagus to the stomach in front of the arch of the aorta is a brilliantly conceived, difficult achievement. It should stimulate all of us, particularly those interested in thoracic surgery.

I do not believe that we should even ponder on Dr. Sweet's results, and should certainly not criticize the mortality in his series. He is dealing with a lesion certain to kill and certain to kill rapidly. If he has extended any of these patients' lives and has increased their comfort, as is obvious from his results, surgery has been truly successful. In dealing with carcinoma of the esophagus in comparison to benign strictures, there can be no choice between early one-stage esophageal anastomosis and multiple-stage surgery.

I think that Dr. Sweet considers this as only a preliminary report, in many ways a report of progress, but the fact that we have among us a man with courage enough to tackle this problem in a large series — and 9 is a large series — deserves commendation.

Dr. David Cheever, Boston: I wish first merely to pronounce the word "magnificent!" During Dr. Sweet's discussion he uttered the words, "if you remember your anatomy." Dr. Sweet does remember his anatomy. I do not believe that he had to bone up on his anatomy before performing these operations.

Harvard Medical School students in the course of their instruction in anatomy have had called to their attention over many years the tremendous importance of the blood supply of the stomach and intestines. The points have been made that it is impossible to impair in the least degree the blood supply of the intestines and that, because there are so few anastomoses, one cannot resect freely; whereas in the stomach at least three fourths of the blood supply can be tied off the remaining fourth being sufficient to carry on the nutrition of the tissues, thus permitting extensive resections. Of course, it is this fact that, among so many others, Dr. Sweet has taken advantage of and that has made these magnificent results possible.

Dr. Richard H. Sweet (closing): Both Dr. Newton and Dr. Fred Lund referred to operability, or at least implied that this was in their minds. Dr. Newton spoke about 9 cases being a large series; as a matter of fact, it is, because before we started doing this anastomotic work, I studied the operability of about 70 consecutive cases of carcinoma of the midesophagus that I had seen, and learned that only 14 per cent of the patients were finally subjected to a radical resection. Of course, the reasons for this are obvious. The principal one is the anatomic relation of the esophagus, these tumors lying opposite the pulmonary veins and arteries and the left main bronchus. Many actually invade these structures or the aorta.

With regard to entering the right pleural cavity, in case some of you wish to take up this type of surgery, the opposite pleura is frequently and of necessity opened, because, as you know, the pleura is reflected from both sides of the esophagus; but one need not pay any attention to this. One can open the right pleural cavity with safety, and nowadays I never bother to close it again, because the anesthetist has the situation under control.

I should like also to reiterate what Dr. Newton said. This is a preliminary report, and the whole subject is in a phase of development.

THE ANTITHROMBOTIC ACTION OF GELATIN*

Preliminary Report

HENRY HAIMOVICI, M.D.,† AND JACOB FINE, M.D.‡

BOSTON

PROPERLY prepared gelatin is now regarded as a satisfactory blood substitute within certain limits for the treatment of traumatic shock.[1, 2] Intravenously administered gelatin, however, has been observed to produce an increased bleeding and clotting time in the experimental animal in deep shock.[1–3] This is also true of albumin and plasma.[3] It occurred to us that if this were also a property of such fluids in the relatively normal state of the organism, they might prove useful in the prophylaxis or therapy of deep venous thrombosis, in place of heparin or dicoumarin, which have serious limitations. Of these fluids the most readily available is gelatin. This report deals with a preliminary experimental inquiry into the capacity of gelatin to prevent thrombosis in veins subjected to injury.

METHOD

The simplest method of producing thrombosis in a vein is by the use of a noxious chemical agent.[4, 5] Acceptable conditions for a study of the production of venous thrombosis by a chemical agent require that a given length of vein that has no branches be exposed to a given concentration of a given caustic agent for a given length of time. A sterile surgical technic is essential for this purpose.

Mongrel dogs weighing 8 to 10 kilograms were given morphine sulfate (1.0 to 2.0 mg. per kilogram) or occasionally a 6.0 per cent Nembutal solution intravenously. Under novocain anesthesia the femoral or jugular veins or both were exposed aseptically. After 2.5 cm. of each vein was carefully liberated from its sheath, two loops of thread were passed around it and the blood was gently milked from this segment. The vessel was then lifted by the threads, and into this temporarily isolated segment a quinine-urethane solution§ was injected through a 25-gauge needle and retained under slight tension within the lumen for periods varying from thirty seconds to five minutes. In most of the experiments a two-minute exposure was used. The fluid was then withdrawn into the syringe and the circulation re-established. At the completion of this procedure the wound was closed in two layers. Histologic examination of veins prepared as described, except for the actual injection of the quinine-urethane solution, showed no injury to the intima or resulting thrombosis.

Intravenous pigskin gelatin solutions¶ were used exclusively. The various samples were fairly homogeneous in their simpler physical properties and chemical composition, with the following representative characteristics: dry weight, 7.17 per cent; ash, 0.95 per cent; sodium chloride, 0.85 per cent; reaction, pH 7.42; bloom, 41.0 gm.; and viscosity, 3.4 at 37.5°C. Most of the solutions were autoclaved at 15-pounds pressure for forty-five minutes, and some for a longer period.

In the course of experimentation, twelve different preparations of gelatin were used. Eight of these exhibited definite antithrombotic action, whereas the other four, prepared somewhat differently, showed little ability to prevent intravascular clotting following injury. In the experiments reported below, only preparations known to be active were employed.

RESULTS

Control Experiments

In 13 dogs the intima of twenty-six veins was exposed to the quinine-urethane solution for thirty seconds. These veins were examined eighteen hours to six days after the operation. Ten veins (38 per cent) exhibited complete thrombotic occlusion, five (19 per cent) contained small nonoccluding thrombi, and eleven (42 per cent) were completely patent (Table 1). Failure to induce thrombosis uniformly in these experiments seemed to be due to the short exposure of the veins to the chemical injury. Accordingly, in subsequent experiments (thirty-one veins in 11 dogs) the exposure was increased to one to five minutes, in most of the experiments the time being two minutes. When the vessels were examined fifteen to forty-eight hours afterward, thrombosis was found in 84 per cent of the injured veins.

Macroscopic examination of the occluded veins showed at the site of injury a thrombus that, as a rule, did not propagate beyond the next proximal and distal branches. In only 2 cases was there found an extensive secondary clot, which in each extended from the jugular vein through the superior vena cava, right auricle and inferior vena cava and stopping at the hepatic veins.

Gelatin Experiments

In the experiments with gelatin the points under consideration were the volume and concentration

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The expenses of this investigation were provided from a grant to Harvard University from the Edible Gelatin Manufacturers Society of America.

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‡Associate professor of surgery, Harvard Medical School; visiting surgeon, Beth Israel Hospital.

§Ampules of quinine-urethane solution were kindly supplied by Abbott Laboratories, North Chicago, Illinois.

¶The gelatin solutions were kindly supplied by the Edible Gelatin Manufacturers Society of America.

of the gelatin solution necessary to prevent intravascular clotting (gelatin does not prevent clotting in vitro), the comparative value of gelatin injected before and after injury to the intima, and the period during which the prophylactic action of gelatin remained effective.

Several series of experiments were carried out with these objectives in mind. In the first series, 50 cc. of gelatin per kilogram of body weight was injected intravenously one to two hours before injury to the veins. In the second series, the same amount of gelatin was given four and a half to nine hours before injury, and in the third series, 25 cc. of gelatin per kilogram of body weight was given one to three hours before injury. In the fourth group, gelatin was given after injury to the veins. The gelatin solutions were given intravenously in a single infusion lasting from ten to twenty minutes at the rate of 15 to 20 cc. a minute.

Gelatin injections before injury. The first series included thirty-five veins in 17 dogs. Thirty veins (86 per cent) were found to be entirely patent, and the remaining five contained small, nonoccluding thrombi (Table 2).

In the second series, thirty-three veins in 12 dogs were used. Fifty-two per cent of the vessels were patent, 16 per cent were partially occluded, and 31 per cent were completely occluded. Further analysis of this series showed that of the twenty veins subjected to the action of gelatin between four and a half and seven hours before injury, only one showed complete occlusion; whereas of thirteen veins subjected to the action of gelatin between seven and nine hours before injury, nine showed complete occlusion.

In the third series, the least amount of gelatin necessary to prevent clotting was investigated. Twenty-five cubic centimeters per kilogram of body weight was injected one to three hours before injury to the veins. Of twenty-one veins in 7 dogs exposed to injury for two minutes, fifteen remained patent and seven were partially or wholly occluded.

In summary, it appears that gelatin has a definite in vivo antithrombotic effect; that when gelatin is

TABLE 1. *Control Experiments.*

Exposure to Quinine-Urethane	No. of Dogs	No. of Veins	Vein Patent	Partial Occlusion of Vein	Complete Occlusion of Vein	Partial and Complete Occlusion of Vein
			%	%	%	%
30 seconds	13	26	42	19	38	58
1-5 minutes:	11	31	16	3	81	84
1 min.	8	0	0	100		
2 min.	21	23	5	71		
3 and 5 min.	2	0	0	100		

TABLE 2. *Gelatin Experiments.*

Type of Injection	Exposure to Quinine-Urethane	No. of Veins	Vein Patent	Partial Occlusion of Vein	Complete Occlusion of Vein	Partial and Complete Occlusion of Vein
			%	%	%	%
Intravenous gelatin, 50 cc./kg., 1 to 2 hr. before injury to vein (17 dogs)	1 min.	11	100	0	0	
	1½ min.	8	88	12	0	
	2 min.	5	100	0	0	
	3 and 4 min.	6	67	33	0	
	5 min.	5	60	40	0	
		35	86	14	0	14
Intravenous gelatin, 50 cc./kg., 4½ to 9 hr. before injury to vein (12 dogs)	1 min.	2	50	50	0	
	2 min.	31	52	16	31	
		33	52	18	30	48
Intravenous gelatin, 25 cc./kg., 1 to 3 hr. before injury to vein (14 dogs)	1 and 1½ min.	7	0	71	29	
	2 min.	21	67	24	9	
	3 and 4 min.	8	25	13	62	
		36	44	31	25	56
Intravenous gelatin, 50 cc./kg., 10 min. to 4½ hr. after injury to vein (14 dogs)	1 and 1½ min.	8	25	62	13	
	2 min.	32	22	13	65	
	3 min.	1	0	100	0	
		41	22	24	54	78
Intravenous bovine albumin, 50 cc./kg., before injury to vein (10 dogs)	1 min.	8	13	25	62	
	2 min.	17	35	34	32	
	3 and 5 min.	3	0	100	0	
		28	25	39	36	75
Intravenous physiologic saline solution, 50 cc./kg., before injury to vein (9 dogs)	1 min.	6	50	17	33	
	2 min.	22	18	14	68	
		28	25	14	61	75

given prophylactically in doses of 50 cc. per kilogram at intervals of one to seven hours before injury to the vein, complete occlusion rarely occurs in veins exposed for two minutes to quinine-urethane; that better protection is afforded by a single intravenous injection of 50 cc. per kilogram of body weight than by one of 25 cc.; and that the protective effect falls off rapidly with time but persists for as long as seven hours.

Gelatin injections after injury. In the fourth series of experiments, the animals received the infusion of gelatin from ten minutes to over four hours after injury to the veins. The results obtained, as recorded in Table 2, show that only 22 per cent of the veins remained patent, 24 per cent contained small, nonoccluding thrombi, and 53 per cent were completely occluded. Hence, gelatin provides no substantial benefit when given after injury to the veins.

To test the specificity of these results, the findings following the injection of another protein solution (bovine albumin) and of physiologic saline solution were observed.

Bovine albumin solution. Fifty cubic centimeters per kilogram of body weight of a 5 per cent solution of crystalline bovine albumin* was injected intravenously one to eight hours before injury to twenty-eight veins in 10 dogs (Table 2). Of the injured veins, only seven (25 per cent) were patent. The remainder showed an almost equal percentage of partial (39 per cent) and complete (36 per cent) occlusions. No definite relation appeared to exist between the incidence of thrombosis and the interval between the infusion and the injury to the veins.

Saline solution. Nine dogs, in which twenty-eight veins were injured (Table 2), received intravenous infusions of physiologic saline solution (50 cc. per kilogram of body weight). The injections were given forty-five minutes to four hours before the vessels were injured. Only seven (25 per cent) of the veins were completely patent. Complete venous occlusions were found in 61 per cent, and partial occlusions in 14 per cent.

Although the percentages of venous occlusion were identical in both the albumin and saline series, complete obstruction in the saline series was almost twice that of the albumin series.

Hematologic Studies

Presumably the effect of gelatin on the thrombotic process involves an alteration in the blood constituents concerned with the coagulation phenomenon. This report deals only with the hematocrit and the bleeding, clotting and prothrombin times.

Hematocrit. All hematocrit determinations were made on citrated blood in Wintrobe tubes, centrifuged at a 2500 r.p.m. for thirty minutes. Blood samples were taken at various intervals before and after the infusion, ranging over an average period of forty-eight hours. The hematocrit did not return to its initial level within this period except in a few cases. The following is a typical example:

Time	Hematocrit
	%
Before infusion	58.0
After infusion:	
5 min.	34.3
1½ hr.	43.0
4½ hr.	50.5
6½ hr.	52.0
23 hr.	50.0
50 hr.	52.0

Maximal hemodilution took place within the first six hours after gelatin infusion. The return of the hematocrit to a normal value is presumably correlated to the disappearance of gelatin from the blood stream; this varies from two to five days depending on the degree of degradation of the gelatin molecule at the time of infusion.[6]

Bleeding time. The normal bleeding time in dogs, determined by pricking the animal's ear, was 2 to 3 minutes. Within ten to thirty minutes after the gelatin infusion, the bleeding time was appreciably prolonged. The maximal effect was present within half an hour after the infusion, but seven hours later the bleeding time was still three or more times normal. Return to a normal level was gradual, requiring more than twenty-four hours.

Clotting time. Determinations of the clotting time were made at room temperature, before and after infusion, by the Lee and White technic. The blood was withdrawn directly from the exposed vein. The average normal clotting time in these dogs was about 3 minutes. After gelatin infusion the clotting time was found to be uniformly prolonged. In some cases the clotting time twenty-four hours after infusion was still twice as long as the control value, an observation at variance with the opinion[7–10] that gelatin exhibits an in vivo coagulant effect.

Prothrombin time. The prothrombin time was determined by Quick's technic, using rabbit brain thromboplastin, on whole and on diluted plasma (25 per cent and 12.5 per cent plasma in physiologic saline solution). The prothrombin time of whole plasma after gelatin infusion was normal, but that of dilute plasma was definitely prolonged. In some cases the prothrombin time twenty-four hours after the infusion had returned to its initial values; in others it was still prolonged.

Pathological Studies†

Specimens for pathological observations were taken at four and a half hours, at twenty-four to seventy-two hours and as late as seven days after injury to the veins, in both the control and the treated series.

In the control series histologic examination in the first twenty-four hours showed the lumen of the vein

*This material was kindly supplied by Armour and Company, Chicago, having been prepared under a contract with the Office of Scientific Research and Development, through the courtesy of Dr. E. J. Cohn of Harvard Medical School.

†We are indebted to Dr. Monroe J. Schlesinger, pathologist of the Beth Israel Hospital, for his help in the study of the material discussed in this section.

to be filled with a fibrin thrombus containing platelets and red cells; there were a loss of endothelium, extensive degeneration of the media, occasional engorged vasa vasorum and hyperemia. At four days the picture was much the same; the vein wall appeared distended and few signs of regeneration were seen except for a few nuclei in the media or adventitia, which again took the stain.

In the dogs treated with gelatin, the patent veins examined one to five days after the injury showed the following changes in the vascular wall. In the first twenty-four to forty-eight hours, as a rule, the cells in the various layers of the vein wall showed a loss of nuclear staining; the engorged vasa vasorum, however, were virtually intact. After five days the vein wall exhibited signs of regeneration and repair of its different layers.

The pathological data are still incomplete, especially with reference to detail in the first few hours after injury and in the successive stages of the healing process in the treated animals.

Summary

An adequate technic of inducing experimental venous thrombosis in dogs has been described. The ability of gelatin to prevent such thrombosis was investigated.

Eight out of twelve samples of gelatin exhibited a definite antithrombotic action when given prophylactically in a single injection. No beneficial effect was obtained when the gelatin was given after injury to the veins.

The bleeding time and clotting time were appreciably prolonged after gelatin infusion. The prothrombin time of whole plasma was unchanged, whereas that of diluted plasma was definitely prolonged.

These data are of a purely experimental nature and should not form a basis for clinical application until more information has been obtained.

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MEDICAL PROGRESS

GYNECOLOGY: CARCINOMA OF THE ENDOMETRIUM

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CANCER originating in the endometrial lining of the uterus has been given varied nomenclatures, such as "cancer of the fundus," "cancer of the body," "cancer of the uterus" and "cancer of the endometrium." Inasmuch as this tumor arises from the cells of the endometrium, it is proper to speak of it as cancer of the endometrium. This tumor is not so frequent as is carcinoma of the cervix, and, until far advanced, it is not nearly so lethal. At the Pondville Hospital since 1927 there have been approximately 1500 cases of cervical cancer and 300 cases of endometrial cancer, a ratio of 5:1. Watkins and Neilson[1] report 216 cases of cancer of the cervix and 43 of cancer of the endometrium, an identical ratio. Masson,[2] of the Mayo Clinic, writes that of 4407 cases of cancer of the uterus in their institution 3273 were of the cervix and 1134 of the endometrium, a ratio of about 3:1. There is a marked difference between the material from public hospitals and that from private practice. The number of cervical cancers is greater among the poor, and endometrial cancer is more frequently encountered in private practice. It is quite possible that, although clinic patients receive excellent obstetric care at the time of delivery, during follow-up the care of the cervix is not so complete and thorough as in the practice of the private obstetrician. This difference possibly explains the comparative absence of cervical cancer in private offices. There are of course differences in diet, hygiene and so forth that could be responsible, but the most obvious contrast lies in the more perfect care of the cervix of the private patient after delivery. Cancer of the endometrium is in most cases a comparatively mild type of tumor, but it can be extremely malignant and rapidly growing. Usually it is nonfatal while within

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the confines of the uterus itself but becomes fatal once it has grown beyond the walls of that organ.

Etiology

The etiology of nearly all forms of cancer is still one of the great mysteries of the human body, and there is no evident cause for this particular type of growth. There have been many attempts to explain the presence of endometrial cancer and many suggestions to this end have been made, but none have thus far proved satisfactory. The late Dr. William P. Graves believed that endometrial cancer and possibly endocervical cancer was due to the irritation of retained secretions, owing to stenosis of the cervix. He thought that poor drainage caused by old cervical scars or cervical atrophy produced a definite irritation and chronic inflammation, and hence cancer. Chronic irritation, together with other factors, may easily have something to do with the formation of cancer. It is not infrequent that pyometrium is noted along with endometrial cancer, and the retention of pus, even though sterile, is almost certain to cause a severe irritation within the uterine cavity. On the other hand, pyometrium is often found in patients with cancer of the cervix and not infrequently in those whose cervical cancer has been treated with radium; yet cancer of the endometrium in these two conditions is extremely infrequent.

It is certain that chronic irritation is not the only cause of this type of cancer, although it is unquestionably present in some. It has been supposed that endometrial cancers may arise on a basis of endometrial polyps, just as intestinal cancer is so frequently found in patients with intestinal polyps. Hirson[3] reported 4 cases in which polyps were found coincidentally with cancer of the endometrium or in which they had previously been removed. Ferris and Dockerty[4] report such a case, and they discuss the criteria for determining that a cancer arises in a polyp: the carcinoma must be confined to one portion of the polyp; the base of the polyp must be benign; and the surface of the endometrium around the base of the polyp must show no malignant change. Their case fulfilled these criteria and must be accepted as a true adenocarcinoma in an endometrial polyp. It may be that other malignant polyps have been found, but it is certainly true that most endometrial polyps are benign and that most cancers of the endometrium do not arise in polyps. The supposed analogy to cancer of the large bowel is not a true one.

Frequently fibroids have been regarded as contributing in some way to the etiology of endometrial cancer. There is no doubt that fibroids are often encountered in patients with endometrial cancer, but by far the vast majority of them seem to have no relation to cancer. If fibroids are due to some abnormality in the reaction of estrin and its sister hormones, the possibility of an association is definite, but a fibroid alone is not an etiologic factor. Masson and Gregg[5] in a series of 590 patients who had been operated on found that 36 per cent also had fibroids. Miller[6] found them in 20 per cent of his cases. Adair[7] believes that 2 per cent of patients with uteruses containing fibroids have an accompanying cancer of the uterus and that 38 per cent of patients with cancer of the endometrium have fibroids. Barns[8] found fibroids in 24 per cent. Watkins and Neilson[1] report fibroids in 38 per cent of their cases of cancer of the endometrium and believe that in some way these tumors are an etiologic factor. Healy[9] found 40 per cent of his surgically treated patients with endometrial cancer also had fibroids, and thinks of this as more than a coincidence, believing that the presence of fibroids indicates that the uterus has tumor-growing possibilities. He advocates removal of the uterus in patients with fibroids over 5 cm. in diameter. Scheffey, Thudium and Farell[10] found fibroids in 38 per cent of all patients treated surgically. Randall[11] believes that the consensus at the present time is that cancer of the endometrium develops just as frequently in a nonfibroid as in a fibroid uterus, and that the presence of a fibroid does not predispose to the development of cancer of the endometrium. His figures substantiate this. If one admits, however, that fibroids are in some way a development of abnormally functioning hormones, — as many surgeons do, — and if one looks at the results of Randall's excellent investigations, one is drawn toward the idea that uterine growths, including fibroids, are the effect of some fundamental disturbance that is also present in the formation of cancer of the endometrium.

Randall shows that patients with menorrhagia at the time of the menopause are three and a half times likelier to develop cancer of the endometrium later than are those who have an uneventful cessation of periods. His figures also show that only 8 per cent of women who did not develop cancer flowed beyond the age of fifty, whereas 35 per cent of those with endometrial cancer did so after fifty-one. No doubt many of these women had fibroids and therefore bled abnormally. He also states that many women with endometrial cancer have not had hot flashes, and do not have vulvar atrophy or senile changes of the vagina. He believes that there is a definite connection between granulosal-cell or thecal-cell tumors of the ovary — both of which produce estrin — and the presence of endometrial cancer. The last phenomenon has been noted by many authors.

All these findings considered together lead one to conclude that fibroids may not be an etiologic factor, but that they and endometrial cancers are produced just as are abnormal bleeding at the menopause and hyperplasia of the endometrium.

Before the evidence for and against a hormonal etiology of this cancer is given, the question of any

other etiologic factor should be clarified. It is well substantiated that cancer of the cervix is frequently found in women who have borne many children, whereas in endometrial cancer the reverse is apt to be true. Barns[8] concludes that multiparas and primiparas are involved in equal numbers but that endometrial cancer comes in the unused organ and cervical cancer in the used. Radium or x-ray treatment as a reason for the occurrence of such growths must be considered. Luker[12] reports a case of his own and points out 14 others in the literature. There is no doubt that radiation may form the base of an epithelioma, for it often occurs on the skin following radiation treatment. Injury of the endometrium due to radium in the uterus may constitute the nidus of an epithelial growth, yet in many of the cases reported by Luker, the tumors came so soon after the radium treatment as to make one think that the tumor was present at the time of the curettage and was missed by the curette. Scheffey[13] collected from the literature 71 cases of cancer following radiation; in 18 the cervix was affected, in 40 the endometrium, and in 13 the location was not stated. He added 20 cases — 7 of cancer of the cervix, 12 of cancer of the endometrium and 1 of myosarcoma. From his analysis of these cases he concludes that errors of omission in either technic or judgment and not the radiation therapy itself were the responsible factors in the subsequent occurrence of cancer. Randall,[11] however, reports 4 such cases a year after treatment with 1000 to 1800 mg. hr. of radium. Corscaden[11] in discussing Randall's paper states his belief that the radiation menopause has no therapeutic value in preventing cancer, but he doubts that it is a cause of cancer. He thinks that intrauterine radium may be a cause of cancer in the uterine cavity, just as it may produce cancer on an epithelial surface in other parts of the body. Cancer of the cervix or upper vagina occurring five to ten years after previous proper treatment of a cervical cancer may be a recurrence or it may be due to the radium treatment itself, and the same applies to cancer of the endometrium.

The question of whether estrin is a responsible etiologic factor in the development of endometrial cancer has not been decided. It is the opinion of most gynecologists that treatment of the menopause in cases with the uterus intact should be carefully thought out, that the dosage of estrin should be small, that the drug should be withheld one week out of every month and that, if withdrawal bleeding occurs two weeks later, curettage should be performed. All authorities admit that estrin is a potent growth-producer and that in certain types of animals one can produce cervical and endometrial cancer. Important evidence is furnished by the facts that Smith[14] has found thecal-cell hyperplasia in a number of cases of cancer of the endometrium, that I have recently observed it in the ovaries of a patient with cancer of the cervix and that many have noted the frequency with which adenocarcinoma of the endometrium is present in patients with granulosal-cell or thecal-cell cancers of the ovary.

Most observers have rarely seen cancer of the endometrium in the castrated. Ingraham, Black and Rutledge[15] note that Dr. G. Van S. Smith has reported 3 cases of cancer of the endometrium occurring fifteen years after bilateral oophorectomy. The facts mentioned concerning fibroids, cancer and bleeding at the menopause, and also the fact that Randall[11] has noted the infrequency of hot flashes and atrophy in women with endometrial cancer, are significant. I have noted the absence of hot flashes in patients with cervical cancer who have received radiation. All these findings should make one hesitate to give estrin or diethylstilbestrol to every patient with a complaint, whether or not it can be attributed to the menopause. Ladin[16] warns that it is not to be taken for granted that bleeding in the treatment of the menopause is due to estrin. Without confirmation by curettage, Scheffey, Farell and Hahn[17] say that when abnormal bleeding is present during the later reproductory, menopausal and postmenopausal periods there is much less justification for prolonged endocrine therapy. They report cases in which endocrine therapy was introduced to control abnormal bleeding without preliminary examination to exclude organic pelvic disease, the result being a delayed diagnosis and treatment of uterine cancer. Corscaden, in discussing the above paper, states his belief that there is a relation between estrogen stimulation and the later development of cancer.

Ingraham, Black and Rutledge[15] quote Dockerty as reporting 3 cases of cancer of the endometrium in 32 cases of granulosal-cell tumor and 1 in 10 cases of thecal-cell tumor, and conclude that the incidence of 10 per cent is more than coincidental. They themselves report 2 cases of endometrial cancer in granulosal-cell tumor and 1 in thecal-cell tumor of the ovary. In the discussion of this paper Stohr reports the case of a patient with cancer of the endometrium who simply had her granulosal-cell tumor removed and who on subsequent curettage had no cancer. Hertig[18] states that at the Free Hospital for Women (Brookline, Massachusetts) at least 18 to 20 per cent of the patients with granulosal-cell tumors and thecomas have an associated carcinoma of the endometrium.

Novak[19] reports a case in which a diagnosis of cancer of the endometrium was made following estrogenic treatment but in which subsequent curettage after cessation of treatment showed no cancer. Ingersoll[20] curetted a patient who had bled following estrogen treatment and the pathologist reported carcinoma of the endometrium; a subsequent curettage two weeks later showed no cancer and intrauterine radium treatment was given; six weeks later the uterus was removed and no cancer was found. Novak[19] advises against prolonged and

excessive treatment with estrogens after the cessation of ovarian function because of the frequent finding of endometrial hyperplasia and cancer. Crossen and Hobbs[21] found that 60 per cent of women with uterine cancer still continue to menstruate after the age of fifty, whereas in a large number of women without uterine cancer menstruation occurs at this late age in only 15 per cent. According to an editorial in the *Journal of the American Medical Association*,[22] these findings suggest that the long-continued action of ovarian hormones may be of significance in the origin of cancer not only of the mammary glands, the cervix and the vagina but also of the fundus of the uterus. Crossen and Loeb,[23] however, state that hormones alone are not responsible and that other factors must be present along with growth-producing factors. Randall[11] writes that Herrell studied the blood estrogens in women with cancer of the uterus in the postmenopausal period and reported no significant high levels. It is agreed, however, that the cause of hyperplasia of the endometrium is persistent, not high, levels of estrin. Jones and Brewer[24] found that of 19 premenopause patients with cancer of the endometrium 11 had cyclic menstruation, and of 9 operated on 8 had functioning corpora lutea. The ovaries may function normally and part of the endometrium may be normal. They believe that cystic changes in the ovaries are incidental and without significance.

From all this material it is evident that the estrins and similar preparations may be indicted in tumor production in both animals and human beings. Definite cancer production in the latter has not been proved, but there is enough suggestion of it to make one careful of excessive and prolonged treatment with estrin. Cancer of the endometrium does occur in patients before the menopause. Wallis[25] reports that Stacey found 36 per cent of his patients to be in the premenopausal stage, Norris and Dunne 30 per cent, and Masson and Gregg 33 per cent.

Cancer of the endometrium spreads by way of the lymphatics and blood vessels and possibly by the vertebral system of veins, as described by Batson.[26] The nodes involved are apt to be higher than those involved in cervical cancer — usually the upper iliac and lumbar nodes or those in the neighborhood of the kidneys. The vagina, the tubes and the ovaries are also attacked. The involvement of any of these organs makes for an extremely poor prognosis. Johnston[27] has advocated dissection and removal of the common iliac, uterine and external iliac nodes in doing a hysterectomy for cancer of the endometrium, but in my opinion this sort of procedure should accompany the operation for cancer of the cervix rather than that for endometrial cancer. Vaginal extensions have been noted by Strachan,[28] who believes that surface spread or submucous lymphatic infiltration is rare; he found vaginal metastases only in cases that were far advanced. In 90 cases, vaginal implants were noted in 12 and no patient survived. I[29] found that vaginal metastases were not infrequent, noting them in 25 (12 per cent) of 206 cases at the Huntington Memorial Hospital. I believe that the extension is not an implantation but is a lymphatic metastasis by way of the cervix, which has a lymphatic connection with the uterus. This form of metastasis may be spread during hysterectomy, either by implantation in the raw vaginal cuff or by pressure on the lymphatics of the fundus. At the Pondville Hospital, radium treatment is given before operation, which is performed six weeks later, and in seven years there has been no case with a vaginal metastasis. The prognosis of patients with vaginal metastases is poor.

Involvement of the fallopian tubes and their role as paths of extension for cancer of the uterus to the ovary and cancer of the ovary to the uterus are discussed by Wallis[25] and by Lynch and Dockerty.[30] All these authors agree that cancer is found in the lumen of the tubes both free and implanted. Philipp and Huber[31] report that in 16 of 62 patients they found extension into the tube. In 9 cases the tumor was free in the tube, and in 1 it was found on the surface of the ovary. Over twenty-six years ago Sampson[32] advocated tying the ends of the tubes as the first step in hysterectomy, and also avoiding dilatation and curettage to prevent forcing cancer cells out through the tubes. Gentle manipulation of the uterus at examination in patients with suspected cancer of the endometrium is universally advised. Lynch and Dockerty[30] believe that the tubes are rarely the pathway of cancer extending to the ovaries or peritoneal cavity, but admit that this is possible. They conclude from anatomical studies that it is likelier that extension takes place by way of the lymphatics or by direct extension.

Involvement of the ovaries by cancer of the endometrium is a definite possibility, and in many hands these cases have done poorly. Barns[33] has reported that 7 of 95 patients had such involvement, and he believes that the prognosis is good, provided that there is no other extrauterine extension. This has not been my experience. Lynch and Dockerty[30] found that in 4 per cent of the operated cases of cancer of the endometrium one or both ovaries were eventually involved with cancer.

Brezina and Lindskog[34] report a total pneumonectomy for discrete tumor of the upper lobe of the right lung following hysterectomy for cancer of the endometrium, with removal of both tubes and ovaries, some years before. The patient recovered, and the tumor proved to be a metastasis from the cancer of the endometrium.

Barrows[35] operated on a patient with cancer of the endometrium who was given radium nine and four years before hysterectomy and who subsequently lived for six years in good health. Taylor, in discussing the paper, reported a patient who had had a dilatation and curettage for adenoma malignum at the age of forty-five, who had had no treat-

ment and who sixteen years later had the same type of tumor. These cases indicate the slow growth of some of the endometrial cancers, but there is always a question whether such patients had cancer or merely atypical hyperplasia.

Pathologic Histology

Cancers of the endometrium are divided by some authors into adenoma malignum and adenocarcinoma, Grades I, II and III. Many omit adenoma malignum and believe that it really represents a Grade I adenocarcinoma. It is my belief that there is no such thing as adenoma malignum and that this nomenclature should be discarded. There is another epithelial tumor of the endometrium that is not often mentioned, namely, adenoacanthoma. This tumor is a combination of malignant adenocarcinoma and malignant squamous-cell carcinoma. It may occur in the endocervix and cervix, as well as in the endometrial cavity. Its treatment is the same as that for any cancer of the endometrium, except that it should never be treated with radium alone, since the results from such treatment are poor. Healy and Brown[36] believe that approximately half the endometrial cancers are adenoma malignum, one quarter adenocarcinoma, Grade II, and one quarter adenocarcinoma, Grades III and IV. Miller[6] thinks that histologic grading helps in the prognosis but is only one of several factors; he is not impressed with the fact that Grades I and II are radiation-resistant. Corscaden[37] believes that tumor grading is less important in radiation cases than in hysterectomy cases. The pathologic histology of these tumors is important only in that they can be distinguished as slowly, moderately fast and rapidly growing tumors and as a combination of adenocarcinoma and squamous-cell carcinoma.

Carcinoma simplex is also reported, but this tumor may be simply an adenocarcinoma growing so rapidly that it is impossible for it to differentiate. Epidermoid cancer of the endometrium is found and probably arises in areas of metaplasia. Such areas are occasionally found in the normal uterus, and it is not difficult to believe that epidermoid cancer might originate in such an area.

Symptoms

The chief symptoms of endometrial cancer are bleeding, discharge and pain. The bleeding may be profuse in the premenopausal period or at the time of catamenia; in the postmenopausal stage, the bleeding is often fairly continuous and small in amount. The discharge is watery and tinged with blood, both before and after the menopause. Pain indicates extension of disease and usually means a poor prognosis. Most patients with cancer of the uterus are in the postmenopausal age group, the most frequent age period being fifty to fifty-nine. Kamniker[38] states that he did not find a single patient under thirty. Scheffey, Thudium and Farell[10] assert that bleeding is the most significant symptom, having been present in 96 per cent of their series. Corscaden[39] found that of 201 patients one third had symptoms for more than one year and half for more than six months before the patients first went to their physicians.

Diagnosis

The diagnosis is made on microscopic examination of the endometrium, either after the uterus is removed or after curettage. The removal of small specimens with the endometrial biopsy curette is not a satisfactory method of making the diagnosis. If the piece of tumor removed shows cancer, the diagnosis is made, but a negative report is not convincing. Ward[40] believes that diagnostic dilatation and curettage is the most valuable method of making the diagnosis and that early diagnosis is essential. Ladin[16] states that in 1914 he reported 3 cases of cancer of the endometrium cured by curettage alone. Previous to his report 18 cases had been reported, and he therefore advises dilatation and curettage previous to operation. If there is a question concerning the presence of cancer in a given specimen, one should not rely on a frozen section but should wait until the tumor has been properly cut and studied. He is opposed to vaginal hysterectomy when cancer is suspected. MacFarlane, Sturgis and Fetterman[41] report an early case in their yearly examination clinic in which the patient was well six years after radium and x-ray treatment, and one in which the patient after the seventh visit was found to have a symptomless fibroid and was operated on elsewhere by supravaginal hysterectomy, a small tumor being found just above the line of removal. The latter patient was well two years later. Supravaginal hysterectomy is not the proper treatment for cancer of the endometrium.

The history and a curettage were the only ways to make a diagnosis of carcinoma of the endometrium before operation until Papanicolaou and Traut[42] in 1941 and Meigs, Graham, Fremont-Smith, Kapnick and Rawson[43] in 1943 demonstrated the practicability of vaginal smears in the diagnosis. Vaginal-smear diagnosis in carcinoma of the endometrium is not so accurate as that in cancer of the cervix. There is no question that the cells exfoliate, but diagnosis from the cells is more difficult. The best percentage of correct diagnosis by this method is between 80 and 85 per cent. According to Papanicolaou and Marchetti,[44] Bourgeois and Cary advised removing material for smears from the uterus by means of a suction apparatus; the former agree that this method has great possibilities. The use of the method of vaginal smears described by Papanicolaou will become of increas-

ing value to clinicians as more and more laboratories are equipped to carry out proper interpretation of the slides.

Treatment

Treatment of cancer of the endometrium may be surgical or radiologic or a combination of both. There is no doubt that nearly all workers in this field believe that the combination treatment is the most satisfactory. Thus, of sixteen writers on the subject, all but two agree that the results are better with the use of radiation and surgery. Three have employed vaginal hysterectomy to a large extent, and one of these always removes the ovaries at the time of the operation. Some prefer to use radiation exclusively, and all admit that good results can be obtained if it is properly given. Masson,[2] with the largest series, gives his immediate mortality for total hysterectomy in cases of endometrial cancer as 4.5 per cent, that for vaginal hysterectomy as 3.2 per cent, that for subtotal hysterectomy as 9.2 per cent and that for radiation as 1.5 per cent. Healy and Brown[36] advocate not less than 3600 mc. hr. of intrauterine radium before operation and believe that 75 per cent of the patients so treated should survive for five years. Philipp and Huber[31] prefer vaginal hysterectomy. All agree that the operative mortality following total hysterectomy should not exceed 2 per cent. Arneson[45] advises x-ray and radium for the operable group and x-ray and radium as for cancer of the cervix in the inoperable group. Crossen[46] believes that preliminary radiation decreases the chance of metastasis. He distributes the radium along a special wire apparatus or packs it in with detached units. Miller[6] advises proper radiation, followed by total hysterectomy six weeks later. Johnston[27] recommends removal of the regional lymph nodes in addition to total hysterectomy. Kennedy[47] has never had a recurrence of cancer following vaginal hysterectomy by the clamp method when there was no involvement of the peritoneal coat at the time of operation. He speaks strongly against dilatation and curettage. Schmitz, Sheehan and Towne[48] found that of 11 patients receiving hysterectomy after full radium treatment 5 were free of cancer. Corscaden[37, 39] believes that there is a chance for improvement in the method of radium application and in the order in which radium, x-ray and surgery are given. He thinks that 60 per cent of the patients operated on today should survive five years. He quotes Heyman as having consistently improved his percentage of cures until in his 1932–1935 group it was 63 per cent. Corscaden obtains some relief from the use of x-ray in pelvic and abdominal-wall extensions. He thinks that the combined treatment should give 80 per cent five-year cures. In his radiated cases 24 per cent showed no cancer when the uterus was removed. He quotes Farras as having 6 of 27 patients without cancer after radium, Donovan and Warren 5 of 46, Martin 3 of 4 and Schmitz, Sheehan and Towne 4 of 5. Corscaden was able to keep 55 per cent of his patients well for five years with radium alone.

At the Pondville Hospital the uterus is measured with a hysterometer, and a gold radon tube is made that fits into a Monel applicator of the same measurement as the uterus. This is left in the uterine cavity long enough to give 3500 mc. hr. of radiation, and is followed by x-ray therapy, if desired. Total hysterectomy is done six weeks later. In few cases has all the cancer disappeared. In most cases the tumor shows marked injury and no vaginal metastases have occurred. It might be argued that six weeks' delay after radiation is too long a time, but with this delay no cancer had advanced beyond what it was before radiation was given, and usually the uterus is definitely smaller. In a few cases evidence of radiation reaction is found on the outside of the uterus or on the surface of the intestine, but no disaster has occurred since its use. Operation is no more difficult in those cases than in those in which radiation has not been given. If technically possible, a good-sized vaginal cuff should be removed. Both tubes and ovaries should always be removed. The dissection of the lymph nodes is not advocated at present, but after it has been done in more cases and the results have been reported it may easily become a part of the operation. For the inoperable cases x-ray and radium in full doses should be given. Great care should be taken to spread the radiation throughout the whole uterine cavity, for every part of it must be radiated if success is to follow.

The results of treatment vary. Arneson[45] found that the average five-year cures from surgery were 55 to 60 per cent and those from radiation in favorable cases 50 to 55 per cent. Miller,[6] treating inoperable cases with x-ray and radium, kept 34 per cent of the patients well for five years. In the operable group his results from radium and total hysterectomy were 71 per cent cures for five years. Masson and Gregg[5] effected cures for five years in 60 per cent of 711 cases and cures for ten years in 48 per cent of 520 cases. Smith[14] reports 58 per cent of 307 cases cured for five years and 45 per cent for ten years. He believes that if a patient survives thirteen years after treatment of this disease, she is cured. Scheffey, Thudium and Farell[10] effected five-year cures in 36 per cent of patients with surgery alone, in 41 per cent with radiation alone and in 38 per cent with surgery and radium. Corscaden[37] found that if the uterus was smaller than an eight-week pregnancy his results were 75 per cent cures for five years, a large uterus giving but 37 per cent results, and that if the cancer was beyond the uterus only 5 per cent of the patients survived five years. Healy and Brown[36] believe that adenoma malignum or low-grade cancer and adenoacanthoma give about the same results. If the uterus is not larger than a two-and-a-half-month

pregnancy and there is no extension, the five-year cures should be 60 per cent. Their five-year cures for 96 patients who could not undergo hysterectomy and were treated with radium was 39 per cent. It is therefore evident that five-year cures of at least 60 per cent should be obtained in the combined treatment of this disease.

Conclusions

Cancer of the endometrium is curable in a large percentage of cases.

The proper treatment consists of radium or x-ray or both, followed by total hysterectomy and bilateral salpingo-oophorectomy, with the removal of a large vaginal cuff, if possible.

Dissection of the lymph nodes has not as yet proved its value, but may do so in the future.

The diagnosis is best made by curettage; endometrial biopsy is not satisfactory.

Estrin in some form is possibly one of the etiologic factors. Endometrial polyps, unlike intestinal polyps, are probably not frequent etiologic factors.

The pathologic diagnosis of adenoma malignum should be discarded.

Cancer of the endometrium is extremely malignant once it has grown beyond the confines of the uterus.

264 Beacon Street

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 31271

PRESENTATION OF CASE

A sixty-five-year-old man was admitted to the hospital because of progressive malaise, anorexia, weakness, weight loss and swelling of the ankles.

The patient had been well and active as a shoemaker until about nine months before admission, when because of malaise and loss of strength he went to a physician. The patient was referred to a thoracic surgeon but failed to seek further medical aid until seven months later. Beginning nine months before admission the tips of the fingers and toes were observed to have become progressively larger. There had been no chest pain, cough, dyspnea or fever. He had experienced periods of pain in the fingers, elbows, hips, knees and ankles over this period. The ankles had swollen progressively since the onset of his illness and caused the most frequent joint pain. The knees became swollen on occasion. Aspirin brought considerable relief, but the taking of these tablets was followed by night sweats. His normal weight was about 125 pounds, and on admission he weighed 105 pounds.

Over the fifteen years before admission he had had vague joint pains that responded to aspirin, but these were unlike the pains experienced during the nine months before entry.

Physical examination revealed a well developed, pale, somewhat wasted and drawn man who was alert, co-operative and in no distress. The superficial veins were prominent over the entire body but were not distended. No superficial lymph nodes were felt. There was marked clubbing of the fingers and toes. There was moderate nonpitting edema of the ankles and feet bilaterally. The chest was symmetrical, with good expansion. The neck was normal. The lungs showed slight dullness to percussion and an area of tubular breathing at the right base posteriorly. There was a small area of dullness and diminished tactile fremitus over the left apex posteriorly. A few fine high-pitched rales were heard at the left posterior base. The heart and abdomen were normal, the liver and spleen not being palpable. A small right direct inguinal hernia was present. The joints of the hands, arms and legs were not enlarged and showed no limitation of motion. The ankles were not red or hot.

The temperature was 100.0°F., the pulse 80, and the respirations 24. The blood pressure was 110 systolic, 60 diastolic.

Examination of the blood showed a white-cell count of 13,000, with 73 per cent neutrophils. The hemoglobin was 11.0 gm. The urine was normal but for an occasional red and white cell in the sediment. The serum nonprotein nitrogen was normal. The protein was 6.5 gm. per 100 cc., the albumin-globulin ratio 1.2, the phosphorus 5.3 mg. per 100 cc., the chloride 91 milliequiv. per liter, the acid phosphatase 3.8 units per 100 cc., and the prothrombin time 36 seconds (normal, 18 to 20 seconds).

X-ray examination of the chest revealed a 10-by-9-by-9-cm. shadow of increased density in the posterior portion of the base of the right lower lobe (Fig. 1). The shadow appeared to be fairly homogeneous in density. An additional shadow measuring 3 by 2 cm. was seen overlying the right third rib laterally. The remainder of the lung fields was clear. The diaphragm was low, and the right half showed some limitation in motion. The bones of the chest appeared normal. Fluoroscopy and Bucky films showed the mass in the right lower chest to move with the lung rather than with the ribs and over a fairly large portion of its circumference it was possible to see what appeared to be the inner surface of a wall. The smaller mass was not seen by fluoroscopy. An intravenous pyelogram was negative. An echinococcus antigen skin test was negative. X-ray examination of the hands and feet showed extensive periosteal proliferation involving the distal extremities of the radius, ulna, tibia and fibula on both sides and several metatarsals and metacarpals.

After the first week the patient ran a low-grade fever. The clinical picture showed no further change. On the fifteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR J. LINENTHAL: The discussion of this case seems to divide itself into two parts: the first is concerned with the primary diagnosis of what was obviously a tumor inside the chest, and the second with the associated hypertrophic osteoarthropathy and clubbing of the fingers, which the patient had to a striking degree.

Hypertrophic osteoarthropathy is apparently a disease similar in character to the process that leads to clubbing of the fingers, although it involves the more proximal joints of the extremities and gets its name from the fact that there are hypertrophic changes in the bone and disturbances in the joints. The symptoms of the hypertrophic osteoarthropathy that this patient manifested were somewhat more striking than what are usually seen. He had pain involving many of the joints. This pain was presumably much severer than the vague joint pains

*On leave of absence.

that he had previously had. The joints themselves were not unusual on physical examination. There was no limitation of motion, no evidence of fluid, and in the ankles, where he had had the most trouble, there was absolutely no evidence of any acute process. He had moderate nonpitting edema of the feet and ankles. This apparently was not due to a collection of fluid, or it would have pitted, but undoubtedly was a manifestation of the hypertrophic changes in the soft tissue that are sometimes seen in this syndrome. The most striking feature of the osteoarthropathy is apparent in the x-ray films.

Clubbing of the fingers and hypertrophic osteoarthropathy can be seen in a great many conditions, but certainly the most frequent association is with diseases of the lung or related structures inside the chest, and undoubtedly that was the association in this case. As a matter of fact, the patient first went to a doctor, not because of pulmonary symptoms, but because of generalized symptoms of malaise, loss of appetite, weakness and weight loss, and at no time during his illness did he have any symptoms referable to the chest.

DR. GEORGE W. HOLMES: The striking thing in the films is the large, round, sharply defined tumor in the chest. The fact that the tumor is so round and smooth and so homogeneous in density puts it in a fairly definite group. I think it would be unlikely for a malignant tumor to reach that size and be as round and sharp. There is no evidence of interference with air flow in or out of the bronchi, and no evidence of involvement of the pleura. The tumor lies posteriorly, as you can see in the lateral view. It would be interesting to speculate whether it contained fat. Dermoid cysts contain fat, and sometimes this can be shown by x-ray. I should say that this tumor does not show any evidence of fat.

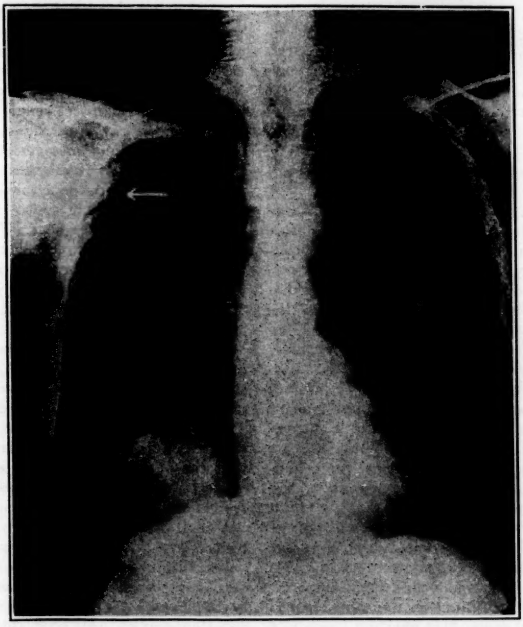

FIGURE 1. *Roentgenogram of the Chest.*
Note the large round lesion in the lower portion of the right chest and the small lesion (arrow) over the right third rib.

The films of the leg and wrist show the characteristic appearance of pulmonary osteoarthropathy, in these cases these changes are the most striking near the ends of the bones.

DR. LINENTHAL: What can be said about the small shadow in the upper part of the right chest?

DR. HOLMES: I do not know what it is.

DR. LINENTHAL: Could it be a metastatic lesion?

DR. HOLMES: In other words, you would like to

think that they are both part of the same process and that the large tumor is also a metastasis?

DR. LINENTHAL: Could the smaller lesion be an unrelated metastasis from somewhere else?

DR. HOLMES: I question whether the large shadow could be a metastasis because of its size. The only tumors that metastasize like that are the sarcomas, and there is no evidence in this story that the patient had sarcoma elsewhere in the body.

DR. LINENTHAL: How much significance can be attached to the statement in the fluoroscopic note that it was possible to see the inside of the wall of the mass?

DR. HOLMES: They were speculating whether this was a cystic or a solid tumor. There are several ways of determining that information, none of which are particularly accurate. If you can see the inside of the wall, that usually means that the tumor is cystic. Sometimes it changes shape on respiration, and that is evidence that it is cystic. Both observations have to be taken with a grain of salt.

DR. LINENTHAL: We have then a large tumor in the chest, and the problem is to decide the nature of this tumor. There appear to be several possibilities. First is the question whether it arose from the chest wall. The observation on fluoroscopy that the tumor moved with the lung and not with the chest wall tends to rule out that possibility. Similarly, as Dr. Holmes points out, there was no involvement of the pleura.

The second question is whether it was a primary lung tumor, and the complete absence of pulmonary symptoms suggests that such was not the case. Having eliminated these two possibilities we are left with the diagnosis of a mediastinal tumor, apparently arising in the posterior mediastinum and extending into the right side of the chest.

The next question is whether it was benign or malignant. Dr. Holmes has mentioned that the general homogeneous smooth appearance suggests a benign lesion. One must pay close attention, however, to the clinical story, and in the same connection consider the question how long the lesion had been present. It seems likely that it had been there for more than nine months. The absence of respiratory symptoms suggests that it was a rather slowly growing process and one would like to suppose, therefore, that it had developed over an even longer period of time. In this connection the question of a congenital cyst might be raised, and although the patient was sixty-five years old, such a lesion is still a possibility. Then again we have some indication to suggest that there was a definite lesion in the chest nine months before admission, because at that time the patient was sent to a thoracic surgeon. It is interesting that the clubbing was first noticed nine months before admission, but presumably it had been developing for a longer period of time. Does this mean that the lesion in the chest began at that time, or that there was some change in a previously existing lesion that had not caused clubbing but because of the change began to do so? I really do not know. The systemic symptoms began at the time the clubbing was first noted, nine months before admission, when he first noted weakness, malaise, anorexia and weight loss. This suggests either a malignant tumor or a low-grade infection, possibly associated with necrosis and hemorrhage inside a previously existing mass. When the patient came to the hospital he had a low-grade fever, a slightly elevated white-cell count and an anemia, which are consistent with either a malignant tumor or low-grade infection.

The small lesion in the chest is interesting and possibly important. It suggests metastatic disease. An intravenous pyelogram was negative, and although the urine showed an occasional red cell, I believe that the negative x-ray films rule out a renal-cell tumor giving rise to lung metastases. The normal acid phosphatase test is against a prostatic carcinoma with metastases to bone, which might also give metastases to the lung. Also there is no x-ray evidence of bone involvement. There is a possibility that the small lesion came from the larger one. There is no evidence of any other primary disease in the body that could have been the source of the smaller tumor. As Dr. Holmes said, it is unlikely that the large lesion is metastatic.

The laboratory data are of no help. All the findings are normal except for the chloride, which was slightly low for no obvious reason, and the prothrombin time, which was definitely abnormal. There is no mention of jaundice, and nothing to suggest that this patient had liver disease. I imagine that the patient received vitamin K before operation. I wonder whether the prothrombin time was redetermined and whether there was any change.

DR. BENJAMIN CASTLEMAN: The test was repeated, and there was no change.

DR. LINENTHAL: Finally, the real problem in this case is the diagnosis of the pulmonary tumor. I do not believe that I am going to be able to make a definite diagnosis. All I am able to do is mention a few of the possibilities.

The lesion said to be most frequent in the posterior mediastinum is a tumor of neurogenic origin, a neurofibroma, which may go on to cystic degeneration and hemorrhage. I can see no way of being sure of such a tumor. This, I believe, may become malignant, but there is nothing in the x-ray appearance of the tumor to suggest that.

The possibility of lymphoma must also be mentioned, but the lesion is too smooth in outline and there is no way of being sure of that diagnosis unless one knew how it responded to x-ray therapy. A congenital cyst can occur at this age. I believe, however, that there is often x-ray evidence of attachment to or encroachment on the trachea or esophagus. There is nothing here to help in that respect. Another possibility is a tumor arising in other tis-

sues, such as a lipoma. Then, there is dermoid cyst, but I know no way of making this diagnosis unless one finds changes of density by x-ray or unless rupture into a bronchus leads to the raising of characteristic material. Furthermore, the patient is too old for such a tumor.

Echinococcal cyst was thought about, but the skin test was negative. It is, I think, positive in a high percentage of these cases.

I suppose one should always mention tuberculosis. It is interesting that on physical examination there was an area of dullness at the left apex, but the x-ray appearance of that region was apparently normal, so that I cannot see how one can go any farther.

I see no easy way of choosing between these possibilities. The best I can do is to put, as my first diagnosis, a tumor of the mediastinum, possibly cystic, with malignant degeneration, associated with hypertrophic pulmonary osteoarthropathy.

Dr. Richard H. Sweet: On the surgical service we have been impressed by the fact that extensive pulmonary osteoarthropathy seems to be associated more frequently with tumors of the lung and mediastinum, usually malignant ones, than with infections. Certainly I think that it would help you to exclude tuberculosis, benign cyst and dermoid cyst. I do not recall having seen osteoarthropathy with either of these conditions. The most extensive pulmonary osteoarthropathy that we have encountered has been in cases of carcinoma of the lung.

Dr. Castleman: Dr. Herrera, will you tell us what you found at operation.

Dr. Rodolfo E. Herrera: At the time of operation the small tumor in the upper chest wall proved to be a lipoma. The large tumor filled the entire right lower lobe. It had not extended to the chest wall, and so far as could be ascertained there were no enlarged lymph nodes in the mediastinum or in the hilus. The fissure between the middle and lower lobes was almost nonexistent, whereas it was almost complete between the middle and upper lobes. It was therefore much easier to remove the middle lobe with the lower lobe than to do a lower-lobe lobectomy, and this was done. The procedure also allowed the resection to be carried out far away from the tumor, which we believed grossly was a fibrosarcoma.

Dr. Sweet: I advised Dr. Herrera to determine first the nature of the tumor in the chest. If it were a metastasis from the large tumor, pneumonectomy would have been unwise.

Clinical Diagnoses

Metastatic tumor of lung.
Hypertrophic osteoarthropathy.

Dr. Linenthal's Diagnoses

Malignant mediastinal tumor.
Pulmonary hypertrophic osteoarthropathy.

Anatomical Diagnoses

Fibrosarcoma of lung.
(Hypertrophic osteoarthropathy.)

Pathological Discussion

Dr. Castleman: The specimen that we received was a large, round, well encapsulated tumor filling almost the entire right lower lobe (Fig. 2). In places

Figure 2. *Photograph of a Cross Section of the Resected Tumor in the Right Lower Lobe.*

it was necrotic. This turned out to be a fibrosarcoma. Whether this was a primary sarcoma of the lung or perhaps metastatic could not be determined grossly. I do not believe, however, that I have ever seen a metastatic tumor that had reached this size.

Do you want to tell us what happened after operation, Dr. Herrera?

Dr. Herrera: The patient had an uneventful postoperative course and was discharged at the end of the second week. From the first day after operation he was completely relieved of his joint symptoms. He volunteered the information that the stiffness and pain were completely relieved and remained so until about two months later, at which time his complaints were no longer centered in the extremities but along the spine and in the left lower quadrant of the abdomen. When x-ray films of the spine were taken, it was apparent that he had wide-

spread metastatic involvement of the vertebras. There was a small nodule at the tumor end of the thoracotomy wound, which on removal showed recurrence of the fibrosarcoma. He went downhill rapidly and died of bronchopneumonia within three or four weeks.

DR. HOLMES: The films that were taken later of the hands and wrist show much less evidence of periosteal reaction; apparently they improved. The appearance in the spine is not too conclusive; there is a mottled appearance, but before committing myself on that I should like to be sure that it was a constant finding.

DR. SWEET: I have had one exception to Dr. Castleman's statement that a single large tumor like this cannot be metastasis. In a patient whom I saw six or seven years ago there was a single metastasis this size in the right lung from a previously resected sarcoma of the breast. I wonder if sarcoma may not be an exception to that statement.

DR. CASTLEMAN: I do not doubt that a metastasis can reach this size, but I do not believe that I have ever seen one.

Unfortunately we were unable to get permission for an autopsy and do not know whether the lesions in the spine were metastatic.

DR. HOLMES: You still do not know whether the one in the lung was metastatic?

DR. CASTLEMAN: Clinically he had no evidence of a primary tumor elsewhere.

DR. MARIAN W. ROPES: The rapidity of the disappearance of bone and joint symptoms is extremely interesting. It came within a few hours after the operation. It is interesting to determine how soon the bone changes disappeared. These films were taken two months after operation and show considerable regression of the osteoarthropathy.

DR. HOLMES: Do the periosteal changes completely disappear?

DR. ROPES: According to the literature that has occurred. We have never had an opportunity to follow them completely enough to see. It is unfortunate that we did not have the chance to see the histologic appearance of the bones in this case.

I agree with Dr. Sweet that the severest pulmonary osteoarthropathy that we have seen has been in cases of malignant disease rather than in cases of infection.

CASE 31272

PRESENTATION OF CASE

A seventy-four-year-old man was admitted to the hospital because of abdominal distress and hematemesis.

The patient was well until a week before admission, when he began to notice abdominal fullness after eating. Flatulence gradually increased, and he became moderately anorexic and experienced periodic nausea. He had a normal bowel movement on the day before admission. On the day of entry he felt more distress than usual. He drank a "rum coke," then went to see his physician. En route to the physician's office he became acutely nauseated and vomited once. While in the office he repeatedly vomited dark fluid containing blood and had an episode of severe agonizing pain radiating from the epigastrium through the lower abdomen to the back and legs. While vomiting he fainted, fell and struck his head on the floor, bruising the left side of the face. He was taken promptly to this hospital.

He had had malaria fifty-three years before entry. He had had pneumonia on two occasions, once fifty-two years before entry and once nineteen years before entry. Six years before admission he had an appendectomy, with drainage, for a perforated appendix. Complicating abdominal-wall and scrotal abscesses were incised and drained. The postoperative period was also thought to have been complicated by a transient toxic hepatitis. He was discharged well five weeks after admission. Three and a half years before admission the patient had had a cholecystostomy for empyema of the gall bladder. At that time a blood Hinton test was positive but a Wassermann test was negative. After three weeks in the hospital he was discharged with a small draining sinus. This ceased to drain a few weeks later, and he remained well until the present illness.

Physical examination revealed a thin man with extremely pale skin and mucous membranes. There were massive periorbital and subconjunctival hematomas on the left side. The abdominal scars were well healed; a moderately sized defect of the abdominal wall was noted below the paramedian incision. Vision was poor. The eyes reacted to light and distance. The heart and lungs were normal. Abdominal examination was essentially negative. There was no tenderness or spasm. No organs or masses were felt. Peristalsis was normal. Rectal examination revealed a normal prostate and no masses or tenderness. A glove specimen of feces was soft and dark and gave a ++++ guaiac test.

The temperature was normal, the pulse 80, and the respirations 20. The blood pressure was 160 systolic, 80 diastolic.

Examination of the blood showed a white-cell count of 18,300. The urine gave a + test for albumin and a green reaction with Benedict's solution; the sediment contained 25 white cells, 2 to 3 red cells and many hyaline and granular casts per high-power field. The serum nonprotein nitrogen was 36 mg. per 100 cc., and the protein 5.6 gm. The chloride and bilirubin were normal. The prothrombin time was 24 seconds (normal, 18 to 20 seconds).

An x-ray examination of the skull showed a fracture of the base of the left zygoma and a fracture of the root of the left maxillary antrum, with depression and clouding of the antrum. There was a questionable fracture of the roof of the left orbit, without additional deformity. In the right occipital area there was an indistinct line of decreased density running in a longitudinal direction for about 9 cm. A barium enema was negative. X-ray examination of the chest was negative, and no free gas was seen below the diaphragm. A gastrointestinal series showed a normal stomach and esophagus by fluoroscopy. The duodenal cap was slightly irregular, and no crater was seen with the fluoroscope. On the film, the duodenal cap showed an area in which the barium pooled, suggesting a crater. A plain film of the abdomen on the next day showed a large amount of barium remaining in the dilated stomach. This dilatation was not present at the time of the gastrointestinal examination on the previous day. There was a small amount of barium in the small bowel, and the colon was fairly well outlined.

At 3:00 a.m. on the third hospital day the patient became apprehensive. The skin was cold and clammy. He complained of severe pain in the abdomen, but this was negative on examination. An hour later he vomited forcefully a large amount of reddish-brown, foul-smelling fluid and the blood pressure was 130 systolic, 75 diastolic. He continued to vomit and passed a soft reddish-brown stool. The vomitus and the stool showed ++++ guaiac tests. At 6:00 a.m. he went into shock, becoming momentarily pulseless and very dyspneic. He vomited again and promptly appeared considerably better,with a strong pulse of 70 and a blood pressure of 130 systolic, 60 diastolic.

At 6:00 p.m. on the fourth day he appeared somewhat improved, with normal temperature, pulse and respirations. About two and a half hours later he was found to have expired. He had passed a moderate-sized, dark-red, tarry stool.

Differential Diagnosis

Dr. George Marks: There is evidence of a variety of lesions in this history. Through it all runs the theme of normal temperature, pulse and respirations, up to practically the last gasp. The question is, Which of the many lesions accounted for his sudden death? The past history contained numerous fairly major episodes: malaria, a drained appendix, cholecystostomy and a positive Hinton test. Yet it says in the beginning that he had been well until a week before admission. Apparently there was no particular loss of well being, at least from the last previous episode to his present entry. He obviously was sick when he arrived, in spite of the temperature, pulse and blood pressure, which presumably was not that of shock, although of course he may have been running a considerably higher pressure before he arrived in the hospital. At entry the pressure was 160 systolic, 80 diastolic.

The first point that seems to carry a good deal of significance is the initial attack in the doctor's office, following a week of gradually increasing abdominal distress. Apparently in the beginning it was not an actual pain as much as a feeling of fullness and discomfort. It was somewhat periodical, and the patient had occasional nausea. He had an acute incident, in that he fainted, fell on his face and head and suffered fractures. I assume from the record that he was not unconscious when he arrived in the hospital, although that is not brought out specifically. The blood pressure and pulse do not indicate any change in intracranial pressure. So I am going to disregard the acute accident, among other things, considering that it had no particular bearing on his death.

He was promptly x-rayed. The stomach was found to be negative, but there was a suggestive lesion in the duodenum at the first examination and at a subsequent one. I presume the second one was a twenty-four-hour plate. I have been told by the x-ray experts that films are of much less value than fluoroscopy, but I should like to see the films.

Dr. Milford D. Schulz: I think that this is probably what was interpreted as a duodenal ulcer. There are no spot films, since we have to depend on the fluoroscopic observation in this day of film shortage. Only a single film of the stomach was made. Certainly there is a marked change in the appearance of the stomach in the film taken the following day. The stomach is greatly dilated, and there is a large amount of residual fluid and barium within it.

Dr. Marks: The question resolves itself into whether this man could have run the course that he did from hemorrhage from such a lesion as a duodenal ulcer. On examination he is described as having a negative abdomen, which he might have had if it were only a small hemorrhage. A large amount of blood in the intestinal tract will produce tenderness and generalized discomfort on palpation, but he apparently did not have those signs. He was not distended. During the course of the first three or four days in the hospital he developed gastric distention and pain, which was relieved by vomiting; this fits in with the distention that caused a disturbance of his intestinal tract from the duodenum on down.

Going back again to his initial attack of pain, the one that was so agonizing that he fainted and fell, I think the possibility of pancreatitis has to be considered. On the other hand, if pancreatitis were present and produced that much pain I should expect that something would have been found on physical examination. Apparently the abdominal examination did not bear out a fulminating pancreatitis.

Did he have a pin-point perforation of an ulcer, with a little fluid escaping now and then? That is possible, and between the escape of fluid he could have had a relatively negative abdomen. Yet, a pin-point ulceration of that sort, even when perforated, does not lead to sudden death.

Shall we pay any attention to the gall-bladder history? There is one point in the laboratory findings, the slightly lengthened prothrombin time, that perhaps represents some disturbance of liver function. Since it was not marked, since the blood bilirubin was not high and since the patient apparently was not jaundiced, it may have been secondary to his general condition. The urinary findings, to my inexpert eye, could represent his seventy-four years, with nephrosclerosis.

There is perhaps one thing that covers his major disorder as well as any, namely, a dissecting abdominal aneurysm. Its first appearance was perhaps before the attack in the doctor's office, which represented the beginning of dissection; later there was disturbance of the innervation of the intestinal tract, and possibly the circulation. I should expect, however, that he would have had more local abdominal signs if he had had a circulatory disturbance of the intestine. I have to consider mesenteric thrombosis, although mesenteric thrombosis certainly has local signs.

I visualize this sequence of events as a dissecting aneurysm that at first progressed slowly and then involved the duodenum, the portion of the intestinal tract that overlies the aorta retroperitoneally, with eventual rupture causing sudden death. There is nothing in the physical examination referring to nerve or circulatory changes in the lower extremities, the blood pressure readings and so forth?

DR. BENJAMIN CASTLEMAN: None were observed.

DR. MARKS: It seems to me that this case is one of death from hemorrhage, and to my way of thinking we have not enough evidence of sudden intra-intestinal or intragastric hemorrhage to explain the picture on that basis.

Sudden hemorrhage may occur from gastritis. Whether the taking of a "rum coke" on the way to the doctor's office was a habit or just to bolster up his morale we do not know. Acute gastritis following bouts of alcoholism can produce massive bleeding. My impression from the history is that there was not a great amount of actual blood, although blood was constantly found in the contents of the stomach and large intestine. I shall rest the case by saying that this was a dissecting aneurysm with final rupture. He had had one positive Hinton test, but whether or not the aneurysm was syphilitic in origin I shall not attempt to say. The x-ray picture may represent ulcer, although I am inclined to believe that the spasm noted by x-ray in the duodenum was secondary to the retroperitoneal lesion.

CLINICAL DIAGNOSIS

Carcinoma of stomach?
Coronary thrombosis?

DR. MARK'S DIAGNOSIS

Dissecting aortic aneurysm, with rupture.

ANATOMICAL DIAGNOSES

Duodenal ulcers, bleeding.
Acute and chronic gastritis.
Hemorrhage into the gastrointestinal tract.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy this patient's stomach was filled with about 700 cc. of fresh clotted blood and the entire gastrointestinal tract was also filled with blood. There were probably two sources for the hemorrhage. He had two duodenal ulcers just beyond the pylorus, one of which was an obvious source of the bleeding; the other source may have been the severe gastritis, which involved almost the entire mucosa. The mucosa was markedly injected, raised and pebbly. I believe that most of the bleeding, however, originated from the duodenal ulcer. That was the complete story.

DR. MARKS: How do you explain the pain in the back and down the middle of the leg?

DR. CASTLEMAN: Dr. Jones has described pain in the back in the duodenal ulcer. I cannot explain the leg pain.

DR. MARKS: Was the ulcer on the posterior wall of the duodenum?

DR. CASTLEMAN: Yes. Those are the ones that frequently bleed.

DR. JONES: Was there a large vessel in the middle of a fairly large ulcer?

DR. CASTLEMAN: The ulcer was not large; it measured 1 cm. in diameter and did have a protruding eroded vessel in its center. Apparently the patient must have bled before admission; the bleeding stopped when he came into the Emergency Ward but began again on the following day.

DR. MARKS: Was it an acute ulcer?

DR. CASTLEMAN: It was an acute erosion of an old ulcer. There was definite evidence of old ulceration.

DR. JONES: There is one thing that may be of some importance. As Dr. Marks pointed out, this patient was seventy-four years old and the story these people tell is frequently different from that of a younger person. It is not uncommon to have bleeding from an ulcer without pain at the time of hemorrhage, but it is not too common to have chronic ulcer and no symptoms whatever. Those in the older age group, however, often have no symptoms and may even perforate without pain. They do not perceive pain as readily as a younger person, and that may change the story a bit.

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HIGH LIGHTS OF THE MEETING OF THE EXECUTIVE COMMITTEE OF THE COUNCIL

One could not have participated in the recent meetings of the Council of the Massachusetts Medical Society without having been impressed with how widespread the Society's activities have become. The vision created by such activities takes this organization out of its semicloistered past and places it squarely in the middle of an active and turbulent world.

The time consumed by the Council in the consideration of these necessary activities has caused many to believe that some change in its method of procedure is called for. Certain steps in this direction have already been taken. The publication of the agenda in advance of the Council meeting is one of them. The formation of the Committee on Council Rules and the subsequent adoption of certain rules of procedure comprise another. It is quite likely that additional rules need adoption, — for example, limitation of the time of debate, — if the conduct of the business of the Society is to keep pace with the fast moving tempo of the times. Rules, however, that are not enforced and in whose enforcement the Council shows no interest will never solve the problem. Such rules are of importance only if they reflect the willingness of the Council to exercise this kind of self-discipline.

The annual meeting of the Council was not held this year because of the restrictions imposed by the ODT. In lieu of this meeting the Executive Committee of the Council met on May 23, 1945. The meeting was called to order at 10:30 a.m. and continued in session, except for a short recess for luncheon, until after 5:00 p.m.

The report of the Treasurer showed the excellent state of the Society's finances.

The report of the Subcommittee on Labor and Industry of the Committee on Public Relations spoke of the committee's conferences with labor and industry and of what it had learned of their respective points of view regarding the distribution of medical care. It emphasized the opportunities that such conferences give to publicize the Society's attempt along these lines through the aegis of the Blue Shield.

The Subcommittee on Public Information of the Committee on Public Relations strained hard at the traditional moorings of the Massachusetts Medical Society. Its report favored the Society's use of paid newspaper and magazine advertising as a means of getting over its messages to the public. That there has been considerable change in the thinking of the Council along these lines is evidenced by the fact that the subcommittee was directed to continue its study and by the further fact that a thousand dollars was placed at its disposal for the purposes of the study.

The supervision of the Medical Information Bureau was turned over to the Subcommittee on

Postgraduate Education of the Postwar Planning Committee.

The report of the Committee on Legislation demonstrated that this committee has made full use of the Society's potentialities. The action of the Legislature on June 6, 1945, in referring to the next General Court a bill that would specifically exempt, until July, 1949, a substandard school from the provisions of the Medical Practice Act seems to bear this out. In this connection, however, it must be remembered that the so-called "Chiropractic Bill" is still before the Legislature. The Society owes much to the vigorous leadership of this committee.

The report of the Committee on Society Headquarters recognized the inadequacy of the space now allotted to the administrative activities of the Society. It offered certain solutions, and was authorized to pursue this subject along the lines recommended.

The Postwar Loan Fund was finally authorized, and an initial sum of $25,000 from the Society's funds was set aside for this purpose. The administrative details have been placed in the hands of a new committee, which has already been appointed by the President.

The report of the Committee on Medical Education showed commendable activity. Under the G. I. Bill of Rights the veteran is entitled to certain opportunities to further his education. Regarding the educational opportunities that relate to the healing arts, there is grave danger that the veteran may spend his time and effort in a school that cannot adequately prepare him in the chosen field. The committee has offered advice in this regard to the Massachusetts Department of Education. The advice was gladly received, and assurance was given of its continued use. This department certifies to the Veterans Bureau the schools that are suitable for training under the bill.

Although the Committee on Rehabilitation offered no report, certain information came to the Executive Committee concerning its activities. The Massachusetts Department of Rehabilitation, as part of its program, is taking notice of those who are in what is termed "a state of static remediable disability." Briefly, this refers to the person who, because of a disability that is static and remedial, cannot take his rightful place in the community. The department proposes to pay the expenses, both hospital and medical, of his rehabilitation. The person's inability to meet the expense involved must be shown, but indigence need not be proved. The Committee on Rehabilitation is at present working with the department on a fee schedule that will cover physicians' services under this heading.

The revival of the New England Medical Council, defunct since 1933, was the subject of a communication from the Rhode Island State Medical Society. The Executive Committee voted to participate.

The President spoke of a meeting that he had recently attended in Michigan. He said that the presidents of seventeen other state medical societies were present. He referred to a resolution that had been adopted at this meeting, part of which called for the creation of a planning committee in each of the states represented and in such other states as wished to participate. It would be the function of these committees to study problems of national interest. They severally would meet from time to time for exchange of views. In the thought behind this movement there was no intention to interfere in any way with the functions or prerogatives of the House of Delegates of the American Medical Association. It was hoped that this type of organization might be of help to the Council on Medical Service and Public Relations of the American Medical Association. The Executive Committee voted to participate in this matter and designated the Committee on Public Relations as the agency of the Society best suited to this purpose.

SECOND ANNUAL REPORT OF THE CHILDREN'S CENTER

A YEAR and a half ago, the *Journal* commented editorially on the most recent addition to Boston's community of medical institutions, the Children's Center in Roxbury, and reviewed briefly its activities and its accomplishments from its establishment in January, 1943.*

The Center has now published its second annual

*Editorial. The Children's Center. *New Eng. J. Med.* 229:732, 1943.

report, a sign that it has passed through its uncertain years of infancy and has emerged into its increasingly fruitful, if still somewhat youthful, period of maturing development. Interested friends and well-wishers can now view its aims and purposes with a better perspective, and no doubt its directors and staff will admit that they, too, can see more clearly the road that they are traveling.

The purpose of the Children's Center is an extremely fundamental one — to go back so far as possible toward the beginning of human behavior patterns, to attempt to analyze the cause of failure in adjustment and to set up machinery by which it can be corrected. According to the introductory words of the report, "the second year of the Children's Center has brought gratifying progress toward its goal as an institute where emotionally disturbed young children may be helped to lead happy and useful lives, and where a fuller understanding may be gained of the factors which make for harmony or disharmony in the development of the human personality."

That referring agencies and the community at large have come to an appreciation of the purposes of the institution is attested by the fact that, although fewer applications for enrollment have been made, the percentage of acceptances, owing to their suitability, has greatly increased.

An important and unique factor in the success of this organization is its employment of the nursery school as a means of studying and retraining the child, thus providing re-education of the emotionally disturbed subject in a group setting. Individual psychotherapy is started at the same time, and conferences with the parent complete the triad of therapeutic measures.

An institution such as this, if it is to achieve its highest degree of usefulness, must, in addition to therapy and research, assume the obligation of teaching. This the Children's Center has done by providing, during the past academic year, field work for two social workers, two students of psychiatric social work, eight nursery-school students and a psychiatric fellow assigned to the Judge Baker Guidance Center. Furthermore, nurses in training at the Boston City Hospital have come two at a time to assist in the nursery school, and members of the staff have been utilized for lectures and seminars given to various groups in the community.

All in all, the Children's Center appears to be successfully and eminently fulfilling the aims that have been conceived by its sponsors, directors and staff.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

McPHERSON — George E. McPherson, M.D., of Amherst, died June 16. He was in his sixty-ninth year.

Dr. McPherson received his degree from Baltimore Medical College in 1904, and became a staff member at the Carney Hospital, South Boston, in 1912. He left there to become neuropsychiatric specialist at the Sturdy Memorial Hospital in Attleboro and later became superintendent at the Foxboro State Hospital. He served for two years as assistant executive officer at the Boston Psychopathic Hospital and assistant superintendent at the Medfield State Hospital. He was superintendent at the Belchertown State School for twenty-one years before his retirement. He was a fellow of the American Medical Association.

His widow, a daughter, a son and five grandchildren survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MAY, 1945

RÉSUMÉ

Diseases	May 1945	May 1944	Seven-Year Median
Anterior poliomyelitis	1	1	1
Chancroid	1	3	*
Chicken pox	1122	2560	1207
Diphtheria	14	21	11
Dog bite	1321	1388	1335
Dysentery, bacillary	19	34	12
German measles	167	381	382
Gonorrhea	484	440	358
Granuloma inguinale	2	0	*
Lymphogranuloma venereum	3	4	*
Malaria	146	68	0
Measles	996	4208	4209
Meningitis, meningococcal	19	42	8
Meningitis, Pfeiffer-bacillus	0	2	2
Meningitis, pneumococcal	5	6	5†
Meningitis, staphylococcal	0	0	0†
Meningitis, streptococcal	1	2	0†
Meningitis, other forms	4	1	1†
Meningitis, undetermined	1	16	10†
Mumps	2222	1459	977
Pneumonia, lobar	261	291	291
Salmonella infections	3	16	16
Scarlet fever	1521	1500	1120
Syphilis	388	439	507
Tuberculosis, pulmonary	319	220	279
Tuberculosis, other forms	19	13	23
Typhoid fever	0	2	2
Undulant fever	2	7	4
Whooping cough	673	324	635

*Made reportable December, 1943.

†Four-year average.

Comment

Diphtheria recorded a welcome reduction of 10 cases from the previous month. Incidence is now only moderately high as compared to the seven-year median.

Meningococcal meningitis showed a slight lowering of its previous high level relative to the seven-year median. Case incidence for the month of May of last year was more than twice that for the present May, and that for May, 1943, four times the present figure.

Mumps maintained its seasonal downward trend.

This is the first time that not a case of typhoid fever was reported in the month of May.

Pulmonary tuberculosis showed an increase and was moderately above the seven-year median. In part, this reflected the results of intensified case-finding programs, which will influence the figures for some time. The great increase in tuberculosis predicted as a result of the war has not materialized.

Geographical Distribution of Certain Diseases

Anterior poliomyelitis was reported from: Camp Myles Standish, 1; total, 1.

Diphtheria was reported from: Arlington, 1; Boston, 5; Camp Edwards, 1; Camp Myles Standish, 1; Chelmsford, 1; Framingham, 1; Lawrence, 1; Melrose, 1; New Bedford, 1; Salem, 1; total, 14.

Dysentery, bacillary, was reported from: Boston, 1; Holyoke, 1; Springfield, 1; Worcester (State Hospital), 16; total 19.

Encephalitis, infectious, was reported from: Yarmouth, 1; total 1.

Malaria was reported from: Boston, 1; Camp Edwards, 81; Cushing General Hospital, 3; Fort Devens, 44; Northampton (U. S. Veterans Hospital), 5; Waltham Regional Hospital, 11, Worcester, 1; total 146.

Meningitis, meningococcal was reported from: Boston, 5; Brookline, 1; Cambridge, 1; Dartmouth, 1; Everett, 1; Haverhill, 1; Lowell, 1; Lynn, 1; New Bedford, 1; North Attleboro, 1; Quincy, 1; Seekonk, 1; Somerville, 1; Springfield, 1; West Bridgewater, 1; total, 19.

Meningitis, pneumococcal, was reported from: Andover, 1; Boston, 1; Cambridge, 2; Northampton, 1; total, 5.

Meningitis, streptococcal, was reported from: Arlington, 1; total, 1.

Meningitis, other forms, was reported from: Boston, 1; Cambridge, 1; Norwood, 1; Worcester, 1; total 4.

Meningitis, undetermined, was reported from: Worcester, 1; total, 1.

Salmonella infections were reported from: Boston, 2; Newton, 1; total, 3.

Septic sore throat was reported from: Boston, 2; Fort Devens, 1; Merrimac, 2; Somerville, 2; Williamstown, 2; Worcester, 1; total 10.

Trichinosis was reported from: Boston, 1; Somerville, 1; Worcester, 1; total 3.

Undulant fever was reported from: Paxton, 1; Pembroke, 1; total 2.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Clinic Consultant
Salem	July 2	Paul W. Hugenberger
Lowell	July 6	Albert H. Brewster
Haverhill	July 11	William T. Green
Brockton	July 12	George W. Van Gorder
Pittsfield	July 16	Frank A. Slowick
Springfield	July 17	Garry deN. Hough, Jr.
Worcester	July 20	John W. O'Meara
Fall River	July 23	Eugene A. McCarthy
Hyannis	July 24	Paul L. Norton

MISCELLANY

SOCIAL AND ENVIRONMENTAL FACTORS IN MEDICINE

The teaching of the social and environmental factors in medicine, as now carried on in medical schools in this country, is being studied by the Association of American Medical Colleges in co-operation with the American Association of Medical Social Workers. A grant to finance the study has been given by the Milbank Memorial Fund. A committee of twenty-five physicians and medical social workers who are engaged in this teaching has been formed to direct the study, under the name of the Joint Committee on the Teaching of the Social and Environmental Factors in Medicine. The co-chairmen are Dr. J. A. Curran, president of the Long Island College of Medicine, and Miss Eleanor Cockerill, associate professor of social case work at the School of Applied Social Sciences, University of Pittsburgh. A centrally located project subcommittee has been set up under the chairmanship of Dr. J. E. Rhoads, assistant professor of surgical research and acting director of the Harrison Department of Surgical Research, University of Pennsylvania School of Medicine. The executive secretary of the study is Miss Harriett M. Bartlett, 49 Fruit Street, Boston 14.

It is the aim of the study to bring together and analyze the experience of a group of medical schools in introducing students to the social and environmental components in medicine. Visits to selected centers will be made by members of the committee. The study is expected to last through 1945, at the end of which time a report summarizing the findings will be prepared.

NOTE

The official corporate name of the Newton Hospital has been changed to the Newton-Wellesley Hospital, the necessary action having been taken by the members of the Corporation and approval thereof secured from the Commissioner of Corporations and Taxation.

BOOK REVIEW

Strophanthin: Clinical and experimental experiences of the past twenty-five years. By Bruno Kisch, M.D. 8°, cloth, 158 pp., with 24 illustrations. New York: Brooklyn Medical Press, 1944, $4.00.

Kisch has done a useful service in summarizing the present status of the use of strophanthin and the history of its introduction in the therapy of heart failure. The small volume is well printed but is expensive.

There are seven chapters and a bibliography of thirty pages. In the preface, the author leaves out, in the opinion of the reviewer, the most important reason why Americans have not adopted strophanthin more generally and routinely, that reason being the excellent experience they have had with the intravenous use of digitalis preparations, which has so sufficed in emergency treatment that strophanthin has been simply an alternative. Kisch speaks of the experience in the United States as being characteristic of that throughout the Western Hemisphere, but in Latin America strophanthin has been in regular usage.

The historical introduction is extremely interesting and is worth while reading in toto. The clinical applications of the drug are clearly presented in Chapter 5.

This book can be recommended to all those interested in the treatment of heart disease.

NOTICES

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, July 12

Friday, July 13

*9:00–10.00 a.m. Medical clinic. Isolation Amphitheater, Children's Hospital.

10:50 a.m. Introduction to Dermatology. Dr. John G. Downing. (Postgraduate clinic in dermatology and syphilology.) Amphitheater, Mallory Building. Boston City Hospital.

12:00 m.–1:00 p.m. Clinicopathological conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

Monday, July 16

*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

Tuesday, July 17

*9:00–10.00 a.m. Medical clinic. Infants' Hospital.

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

Wednesday, July 18

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

September 17. American Public Health Association. Page 752, issue of November 30.

October 1–6. Mediocolegal Conference and Seminar. Page 776, issue of June 28.